CRYPTORCHISM

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PREFACE

The last two or three decades have witnessed considerable progress in our understanding of the problem of the undescended testis These advances have resulted from the discovery of the pituitary-gonadal relationship and from the observance of the effect of the administration of pituitary-like products to cryptorchid boys Improvement in the technic of orchiopexy, based on sounder surgical principles, has resulted in indisputably better cosmetic effects in the hands of a larger percentage of surgeons Furthermore, there is increasing recognition of the need for obtaining a satisfactory functional result, and the importance of follow-up fertility investigation is being emphasized. Unforunately, such investigations require postponement until adolescence or until the problem of infertility arises after marriage

On the other hand, testicular biopsy offers a method of observing viable testicular tissue at any age, making available, whenever desired, accurate information regarding the degree of damage incurred by the testis, as well as the changes brought about by therapy These advances have clarified considerably the problem of cryptorchism but have not contributed to greater agreement on the subject by the two major schools of thought Briefly stated, these two divergent concepts assign the spermatogenic deficiency of cryptorchism to either a congenital or an environmental defect

The need for further clarification and for agreement on

major principles is unquestioned, but our fund of knowledge is perhaps still insufficient for such a desirable goal. The writing of this small volume was undertaken in order to compile the published data, to analyze further the clinicopathologic aspects of cryptorchism and the need for correcting the anomaly, and ultimately to arrive at conclusions which will serve to draw together the two schools of thought rather than to widen the gulf between them. If these aims are accomplished even partially, the authors will stand well rewarded for their labors. If the entire subject has been clarified, this volume should interest and assist the general practitioner, pediatrician, endocrinologist, and surgeon in the management of the anomaly.

We gratefully acknowledge the assistance afforded by Dr. David R. Meranze, Director of Laboratories of the Einstein Medical Center, Southern Division, who contributed considerably to our understanding of the normal and of the pathologic histology of the testis, and who granted us the use of the laboratory facilities.

We are grateful to Dr. S Leon Israel whose helpful suggestions, arising from his own vast experience with manuscripts, have served to make this monograph as readable as it is

We sincerely appreciate the cooperation of Mrs Eunice Stevens of Paul B Hoeber, Inc , whose assistance during the final stages of preparation of the manuscript was most welcome

Finally we are indebted to the Division of Research Grants, National Institute of Health, Bethesda, Maryland, whose grant, A-261, *helped to defray the cost of the investigative* work reported herein

C. W. C.
W. W.

CRYPTORCHISM

chapter 1

INTRODUCTION

The causes and the management of cryptorchism have been debatable issues, in spite of all the literature on the subject, since the anomaly was first described. A question pertaining to the subject still evokes a variety of opinions, some of which are actually contradictory. When should treatment be initiated? Answers range from "As soon after birth as the diagnosis is established" to "No treatment until just before puberty." How effective is endocrine administration? Answers: "Effective only in migrating testes," or "Effective in inducing descent of about 60 per cent of undescended testes." What are the results of orchiopexy? Answers range from "Perfect cosmetic effect with retention of cremasteric reflex" to "Spermatogenesis remains depressed in all cases," or "Orchiectomy is preferable to orchiopexy."

Incidence

Cryptorchism occurs often enough to merit the attention of the entire medical profession, particularly of those faced with the problem of determining its management. Its frequency is said to be 10 per cent in the newborn, 2 per cent at age 1, 1 per cent at puberty, and 0.3 per cent in the adult.[2,3,4,8] The reduced incidence, especially in the first year of life, is the result of spontaneous descent rather than of treatment. Such statistics should act as a deterrent to anyone advocating early surgical correction. However,

recent figures from the adult population are not as cheering. While U. S. Army statistics of World War I show an *incidence of* 0.3 per cent, those of World War II give a surprising incidence of 0 75 per cent for 10,000 consecutive inductees.[1] These figures include unilateral as well as bilateral cryptorchism and are therefore not indicative of ultimate sterility of the individual. However, assuming a 5:1 ratio[5] of unilateral to bilateral cryptorchism, approximately 2 of every 1000 (0.2 per cent) adult men in the United States are sterile because of bilateral cryptorchism.

Contradictory Viewpoints

Many excellent reviews of this subject have been published Notable in recent years are those of Wangensteen in 1927,[7] Rea in 1939,[6] and Bishop in 1945[2] These authors were faced with the problem of reviewing a voluminous *literature full of contradictory statements. The many points* of view which they discovered were frequently so much at variance that great difficulty was encountered in arriving at a common denominator

At the present time, we find ourselves left with the choice of either cataloguing all of the opinions expressed in some 2000 publications or of making a somewhat dogmatic selection reflecting our own point of view To list all of the authors and their varied opinions would lead to confusion rather than clarity, to extract a single statement out of the mire of implications might sacrifice accuracy for the sake of lucidity and conciseness *Perhaps a satisfactory compromise* which is here adopted is to cite the various viewpoints in an orderly fashion and whenever possible, to follow these by a summation and a discussion of our own conclusions

There are two main points of view on the subject of the undescended testis (1) that it is an inherently "sick" testis lacking the capacity for normal development and that its failure to descend into the scrotum reflects this abnormality. (2) that it is a potentially normal testis hampered

in its development by its unfriendly environment, and that a satisfactory orchiopexy will restore it to functional normalcy.

The implications of the first viewpoint are that orchiopexy neither improves spermatogenesis nor prevents malignancy. Indications for the operation are thus limited to a desire to correct an associated clinical hernia or to prevent psychic disturbances resulting allegedly from an empty undeveloped scrotum. In the absence of these relatively infrequent complications, clinical observation without treatment might be advocated, or else orchiectomy might be performed as cancer prophylaxis On the other hand, those who accept the second opinion advocate gonadotrophin administration and, that failing, recommend orchiopexy. Those holding this view are thus attempting to develop an operative technic which will permit proper placement of the testis into the scrotum without injury to its blood supply or to its movability. These two schools of thought are at variance. A common meeting-ground is desirable and essential

Importance of Testicular Biopsy

In the past the results of orchiopexy were judged by the postoperative position and size of the testis. Only in the case of bilateral cryptorchism could semen examination be used as an index of the benefit of the operation The introduction of testicular biopsy has presented us with a direct method of determining the changes effected by orchiopexy. One can now, by serial biopsies during and after operation, obtain an accurate kinetic picture of the progressive changes in the seminiferous tubules. In the case of the child, one need no longer wait until he reaches adolescence to evaluate results of operation Biopsies at varying times after operation will more accurately determine the degree of improvement in spermatogenesis resulting from the scrotal position of the testis Furthermore, comparative histologic study of

the undescended and of the scrotal testis at various ages will disclose more precisely the time at which deleterious effects of malposition begin. Such information will therefore also be of great value in determining the age at which treatment should be initiated.

Our entire investigation and ultimate conclusion have been based on the findings disclosed by testicular biopsy. As a matter of fact our initial interest in this subject was stimulated by the performance of testicular biopsy in a series of infertile and sterile adults who had been subjected to unilateral or bilateral orchiopexy at various ages. The end-results as far as spermatogenesis was concerned were so poor that re-evaluation of the entire procedure appeared to be in order. In at least 20 per cent of the testes, the blood supply had been sufficiently interfered with to produce total atrophy—auto-orchiectomy. In most of the other testes the seminiferous tubules presented the picture of aspermatogenesis. In a small number, some seminiferous epithelium was preserved but cellular development had rarely progressed beyond the primary spermatocyte stage In only a rare instance did a testis show normal tubular maturation, but even in these the number of normal tubules was insufficient to produce an adequate number of spermatozoa and even relative fertility These testes had been brought into the scrotum by many surgeons employing various technics Either the undescended testis was inherently abnormal, lacking the capacity to develop even when placed in the scrotum, or operation was performed after the testis had suffered irreparable damage, or the surgical technic was faulty.

The thought occurred to us that a study of the histologic appearance of the undescended testis at various ages would afford added information on the optimum time for orchiopexy The next logical step was to re-examine the testis within four to six months of orchiopexy in order to determine the *immediate effects of operation* This portion of the

study proved to be especially instructive in instances of unilateral cryptorchism in which the normally descended testis could be used for comparison We soon realized that there was insufficient information available on the histologic picture of the normal child's testis, so that the study of cryptorchism was momentarily interrupted in order to afford time to obtain an accurate picture of the normal testis from birth through adolescence. These studies have already been reported but the data have also been employed in our analysis of the results herein presented.

During the course of our investigation, spontaneously descended testes as well as testes which descended following gonadotrophin administration were subjected to biopsy. These results are also included in the present study.

Nomenclature

The terms employed in the text are those preferred by standard dictionaries. However, we have tried to avoid being purists in terminology *Testis* and *testicle* have identical meanings and although the former is preferred, both terms are used interchangeably. *Orchiopexy* is grammatically preferable to *orchidopexy*, the former is used here even though the term *orchidopexy* appears to be more universal. The terms *cryptorchism*, *undescended testis*, *retained testis*, and *nonscrotal testis* are indentical in implication and are intended to indicate that the testis has not descended normally into the scrotum To indicate position of the undescended testis, the terms *abdominal* or *intra-abdominal* are employed, serving to designate that testis which has not even entered the inguinal canal, the terms *inguinal* or *canalicular* are used for that testis situated in the inguinal canal, and the term *upper scrotal* is employed for the incompletely descended testis that has passed beyond the external inguinal ring An *ectopic testis* is one which has been diverted from its normal pathway through the inguinal canal, completing its descent to a position outside of the scrotum.

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chapter II

EMBRYOLOGY: THE MECHANISM OF DESCENT

The urogenital system of organs is developed from the intermediate cell mass of the mesoderm or nephrotome. Tubular growth within the nephrotome causes a ventral thickening which bulges into the primitive abdominal cavity. This thickening is termed the urogenital fold or Wolffian ridge. As growth continues, the Wolffian ridge produces a distinct projection into the peritoneal cavity, known as the urogenital ridge or Wolffian body. At the fourth week of embryonic development, there appears on the anteromedial surface of the Wolffian body a mesothelial thickening which is the anlage of the gonad From this, the testis in the male and the ovary in the female ultimately develop As the gonad enlarges, grooves develop on its lateral and medial aspects, thus separating it from the parent Wolffian body As a result, the gonad, except for a slender stalk termed the mesorchium, lies free in the peritoneal cavity[4,21]

GROWTH

At this stage, the testis consists of two layers of germinal epithelium, a central, loose cell mass, and a peripheral compact layer The central cell mass develops into an inner and an outer portion The inner portion becomes arranged

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descends behind the patent processus vaginalis to lie in its normal physiologic position at the bottom of the scrotum. It is important to note that descent of the testis is independent of the descent of the processus vaginalis The testis neither pushes the processus vaginalis down in its descent, nor is it pulled down by it. Later, just before birth, the upper part of the processus vaginalis closes and its obliteration extends downward, with the result that the testis lies in a cavity enveloped by peritoneal tissue, the tunica vaginalis testis, which is completely separated from the peritoneal cavity. The scrotum develops when the testis descends into it.[3]

Mechanism of Descent

The testis originates as an upper abdominal organ, as evidenced by the origin of its blood supply and its early embryologic position. During the third intrauterine month its cranial attachments atrophy while its caudal portion continues to grow, so that it comes to lie in the iliac fossa [19] Its descent through the inguinal canal into the scrotum is a phenomenon which is not well understood

Role of the Gubernaculum

The discovery of the human gubernaculum is attributed to Albrecht von Haller,[24] who first described this structure in 1749. In 1904, Eberth,[6] after extensive research, stated that shortening of the gubernaculum attained both by contraction of its smooth muscle and by retrogressive shrinkage causes descent of the testis This theory supported the previous observation of Hunter,[9] who had arrived at similar conclusions More recently Lewis,[10] Rolnick,[16] and Lowsley and Kirwin[12] have accepted the gubernacular theory. But many other observers believe that gubernaculum is not the agent behind the descent of the testis Rost[17] and Bailey[1] state that the gubernaculum acts only as a guide for proper descent of the testis Wells[25] asserts that the gubernacular

into branched and anastomosing cords from which are later developed the seminiferous tubules. The outer portion differentiates into the tunica albuginea. The peripheral layer ultimately becomes the visceral coat of the tunica vaginalis testis.

Early in the fetal life the testis occupies a position in the midportion of the abdominal cavity behind the peritoneum It is connected to the anterior abdominal wall by a fold of peritoneum termed the inguinal fold, which fuses with a peritoneal fold of the anterolateral abdominal wall called the inguinal crest. Within these folds the gubernaculum testis makes its appearance as a slender band of musculofibrous tissue. It begins to form at about the third month of embryonic development and, by the fifth month, has become a thick cord[12] As fetal development continues, the lower portion of the gubernaculum becomes thicker while the upper portion, that between the anterior abdominal wall and the testis, ultimately disappears. A few of the distal fibers, leaving the main band of the gubernaculum, extend to the medial aspect of the thigh and the perineum.[5,8]

DESCENT

As development continues, the testis assumes a progressively lower position and by approximately the third month is at or near the internal inguinal ring A peritoneal tube, known as the processus vaginalis, projects itself downward through the anterior abdominal wall, forming the inguinal canal, and emerges at the external inguinal ring, eventually reaching the bottom of the scrotum In its course it pushes before it a portion of the transversalis fascia, the internal oblique muscle, and the aponeurosis of the external oblique muscle These layers then become known as the infundibuliform fascia the cremaster muscle, and the intercolumnar fascia respectively By the end of the eighth intrauterine month, but *occasionally not until birth, the testis,* together with the vas deferens and the spermatic vessels,

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fibers, following the developing processus vaginalis, are not attached to the scrotal wall and thus play no active role in the descent of the testis. He found that the gubernaculum is attached distally to the fascias of the scrotum which are not immovable structures and cannot therefor act as an anchor. Wells and State[26] showed experimentally in rats that even if the gubernaculum were severed, descent occurred in three-quarters of the animals, and Vanverts[23] demonstrated an absence of fixation by the gubernaculum in many normally descended testes.

Endocrine Aspects

It is now generally accepted that the gonadotrophic hormones play a part in providing the stimulus for testicular migration Engle's[7] experiments with immature macaques demonstrated such a definite hormonal influence on the descent of the testis This was supported by the work of Lombard[11] with the marmot, who arrived at similar conclusions Rost[17] prevented testicular descent in rodents by hypophysectomy Engle[7] also found that chorionic gonadotrophin is present in abundance in the maternal circulation from the seventh week to the ninth month of fetal life, when descent of the testis normally takes place. Endogenous gonadotrophic hormone is found in the urine of boys in appreciable quantities beginning at age 10, and increasing through puberty and adolescence This coincides with the large incidence of spontaneous descent noted at this age [22] Clinically, Schapiro[19,20] first applied this theory to the treatment of boys with nondescent, reporting favorable results This was followed by many enthusiastic papers reporting a high incidence of testicular descent following the administration of the hormone We[3] have observed that the fetal and newborn testis displays unusual development because of maternal gonadotrophic hormones, and it is at this time that descent normally occurs

Inherent Descent Factor

It is possible that there is some factor inherent in the developing testis that encourages and controls its descent. In hibernating animals such as the woodchuck, hedgehog, marmot, and mole, the testes are withdrawn into the abdomen during the winter and redescend during the mating season. The germinal epithelium atrophies during the period of withdrawal and regenerates with recurring descent.[13,15]

These observations demonstrate that the testis has an inherent ability to respond either to external stimulants, such as changes in season, or to internal stimulation such as that brought about by variations in the quantity of gonadotrophin secretion. On the other hand, Martins,[14] substituting paraffin for the inguinal testis, observed that the administration of chorionic gonadotrophin caused its descent also. This experiment supported the theory that the testicular mass is moved along the inguinal canal by a mechanism which is totally independent of its own function. It is difficult to understand these results, in that one would expect that further migration of the substituted paraffin would be hampered by scar tissue resulting from the experimental surgery

In summary, there appears to be a multiplicity of factors playing a role in the normal descent of the testis. The essential elements comprise a normal testis, an adequate amount of maternal chorionic gonadotrophin, and a structurally normal inguinal canal and scrotum If any of these factors is absent or abnormal, descent into the scrotum does not occur

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It is possible that there is some factor inherent in the developing testis that encourages and controls its descent. In hibernating animals such as the woodchuck, hedgehog, marmot, and mole, the testes are withdrawn into the abdomen during the winter and redescend during the mating season. The germinal epithelium atrophies during the period of withdrawal and regenerates with recurring descent.[13,15]

These observations demonstrate that the testis has an inherent ability to respond either to external stimulants, such as changes in season, or to internal stimulation such as that brought about by variations in the quantity of gonadotrophin secretion On the other hand, Martins,[14] substituting paraffin for the inguinal testis, observed that the administration of chorionic gonadotrophin caused its descent also This experiment supported the theory that the testicular mass is moved along the inguinal canal by a mechanism which is totally independent of its own function It is difficult to understand these results, in that one would expect that further migration of the substituted paraffin would be hampered by scar tissue resulting from the experimental surgery

In summary, there appears to be a multiplicity of factors playing a role in the normal descent of the testis. The essential elements comprise a normal testis, an adequate amount of maternal chorionic gonadotrophin, and a structurally normal inguinal canal and scrotum If any of these factors is absent or abnormal, descent into the scrotum does not occur

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fibers, following the developing processus vaginalis, are not attached to *the scrotal wall and thus play no active role* in the descent of the testis He found that the gubernaculum is attached distally to the fascias of the scrotum which are not immovable structures and cannot therefor act as an anchor. Wells and State[26] showed experimentally in rats that even if the gubernaculum were severed, descent occurred in three-quarters of the animals, and Vanverts[23] demonstrated an absence of fixation by the gubernaculum in many normally descended testes.

Endocrine Aspects

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1. Abnormalities of the cremaster muscle
2. Abnormalities of the processus vaginalis testis

E. Gubernaculum:
1. Absence
2. Faulty insertion

F. Pathway:
1. Abnormalities of the inguinal canal
2. Abnormalities of the inguinal rings
3. Abnormalities of the scrotum

II. Testicular deficiency

A Endocrine:
1. Hypopituitarism—secondary hypogonadism
2. Primary hypoganadism

B. Genetic or familial

C. Intersexuality

Mechanical Abnormalities Interfering with Normal Descent

INTRA-ABDOMINAL FACTORS

Intra-abdominal factors for the most part originate prenatally. They include mesorchial deficiencies, peritoneal adhesions, and abnormal intrauterine positions of the fetus

Abnormalities of the mesorchium causing testicular nondescent have been described by Eccles.[22] He observed that a long mesorchium results in failure of the testis to engage the ostium of the processus vaginalis, so that the testis hangs freely in the abdominal cavity as an intraperitoneal organ. *Peritoneal adhesions* have also been listed as a common cause of testicular retention[11,16 57] Such adhesions are allegedly caused by peritonitis occurring early in postembryonic life An *abnormal position of the fetus* in utero—such as abnormal flexion of the thigh—is said to compress the inguinal canal and thus to prevent testicular descent.[27, 51]

Such theories may be acceptable for an occasional case of cryptorchism but they are obviously inadequate as explanation for testicular nondescent in many cryptorchid newborns who appear otherwise normal. Evidence of prenatal

chapter III

ETIOLOGY

Many theories have been proposed to explain the failure of testicular descent, each appears to have some merit, but no single one covers every situation. Two major divisions may be established. (I) mechanical abnormalities interfering with the transport of an otherwise normal testis; and (II) testicular deficiency—either primary or secondary hypogonadism—resulting in either a lack of impetus to descend or a failure of the hypoplastic testis to respond to a normal impetus

Classification

These major divisions may be subdivided as follows:

I Mechanical abnormalities
  - A. Intra-abdominal:
    1. Deficiencies or abnormalities of the mesorchium
    2. Peritoneal adhesions
    3. Obstruction to passage caused by abnormal intrauterine position of fetus
  - B. Spermatic cord
    1. Short spermatic blood vessels
    2. Short vas deferens
  - C. Testis
    1. Structural anomalies of the testis
    2. Abnormalities of the epididymis
  - D. Coverings of the spermatic cord and testis

the testis and epididymis, and *hermaphroditism* preclude normal descent.

COVERINGS OF THE SPERMATIC CORD

Thickening of the cremaster fibers which thus form adhesive bands has been described as a cause of retention of the testis. Kurtzahn[29] found it the most prevalent cause for retention in his report of 118 orchiopexies. Moore and Tapper[35] have also attached great importance to this cremasteric anomaly. Sebileau and Descomps[17] attribute failure of descent to a *lack of elasticity of the cremaster muscle fibers.* Campbell[13] stresses *cremasteric hyperactivity* as a cause of nondescent. Stefko,[40] finding high incidence of nondescent among starving children, attributed this to a *short cremaster muscle* which was merely part of the incomplete development of the abdominal musculature. This was substantiated by de Campos,[19] who found that testicular retention was much more common among undernourished children. Experimentally, Manning[34] observed that animals fed a diet deficient in biotin were uniformly the victims of cryptorchism. Lewis[30] has shown that section of the genitofemoral nerve which innervates the cremaster muscle results in testicular nondescent in rats, and has postulated that the cremaster muscle draws the testis through the inguinal canal into the scrotum

ABNORMALITIES OF THE PROCESSUS VAGINALIS TESTIS

As stated in Chapter II, the development of the processus vaginalis and its descent into the scrotum occurs independent of and generally precedes, testicular descent. Failure of development of the processus vaginalis is accompanied by testicular retention and its aberrant extension results in ectopia testis Failure of obliteration of the processus vaginalis results in congenital hernia

peritonitis is rarely observed in cryptorchids, and abnormal fetal positions would not account for postnatal failure of testicular descent.

SHORT SPERMATIC CORD

Some observers believe that many cases of nondescent are caused by inadequate length of the several structures of the spermatic cord. Büdinger[11] observed that the vas deferens is always long enough but that the *spermatic vessels,* particularly the internal spermatic artery, *are too short for complete descent.* This theory is popular and frequently appears in the literature.[6,38] However, Bramann[9] reported a case in which the *shortness of the vas deferens* appeared to be the sole cause for the incomplete descent. Basilico[4] never observed short spermatic blood vessels, but did find a short vas deferens which required careful dissection. Others have stated that elasticity of the vas deferens is the cause of *testicular retraction and nondescent.*[24]

Our own observations, coupled with those of surgeons of great experience with orchiopexy, are in accord with the supposition that a short internal spermatic artery often prevents testicular descent. This accounts for the difficulty encountered in obtaining sufficient cord length for the proper placement of the testis at the bottom of the scrotum, but does not remove responsibility from the testis per se. There is a generally recognized biologic axiom that an organ develops as adequate a blood supply as it requires. In other words, it is not the fault of the artery but the fault of the testis which, by its failure to descend, makes no demands for elongation on the internal spermatic artery.

STRUCTURAL ANOMALIES OF THE TESTIS

Congenital abnormalities of the testis and epididymis have been cited as a cause of testicular retention. These findings are rare and are for the most part intra-abdominal. Defects such as *fusion of both testicles, failure of union of*

gubernaculum may be deviated in its course and may become lodged in one of the many pouches described by McGregor, such as the *superficial ring pouch*, the *scrotal pouch*, the *perineal pouch*, or the *crural pouch*. In all of his cases of cryptorchism and ectopia he observed either an absence of the third inguinal ring or the presence of fascial pockets and ridges which then trapped the testis, preventing further descent. McGregor's theory appears acceptable for those undescended testes which have passed beyond the external inguinal ring but which have either stopped short of the scrotum or have been directed into other channels. However, the theory does not take into account those testes which are intra-abdominal or intracanalicular.

Browne[10] described an inguinal pouch which lies superficial to the external oblique fascia, forming a bed for 80 per cent of the undescended testes which he observed. Basilico[4] concluded that too early closure of the fascial planes in the *inguinal canal* played an important role in causing nondescent. Meyer[38] and Lazarus and Marks[31] suggested *malformations of the scrotal sac* as a causative factor. Campbell[13] thinks that in some instances the testis is of greater size than the inguinal canal, and Wells and State[55] believe that a small external inguinal ring is occasionally the sole explanation for a canalicular testis

Testicular Deficiency

The supposition that failure of descent is caused by an inherent fault in the testis or any of the other glands of internal secretion has been in the foreground for a long time Hunter[28] believed that the undescended testis is an imperfect organ and that it therefore does not migrate in a normal manner Many others, including Bland-Sutton,[7] Griffiths,[25] Coley,[17] Uffreduzzi,[52] and Schinz and Slotopolsky[48] have also concluded that the primary cause of cryptorchism lies in the testis itself Anvray[2] states that nondescent is due to an arrest of development of the testicular

GUBERNACULUM

The discovery of the gubernaculum by Albrect von Haller[54] in 1749, led to considerable controversy concerning its role in the descent of the testis. Eberth[21] concluded that shortening of the gubernaculum caused testicular descent. Following this report, many observers enthusiastically accepted this theory. However, many instances of normal testicular descent in the absence of a gubernaculum have been described. Authors such as Rost,[44] Bailey,[3] Wells and State,[55] and Cabot[12] believe that the gubernaculum does not play an active role in the descent of the testis. They cite the fact that the gubernaculum is attached distally to the fascias of the scrotum, which are not fixed structures, and that its shortening could just as well pull the scrotal fascias upward as promote testicular descent.

Lockwood[32] described five gubernacular tails which terminate in the scrotum at the pubic bone, in the perineum, in the femoral and superficial inguinal areas, and cited these as a cause for *ectopia*. Bishop[6] confirmed Lockwood's investigation, demonstrating well-formed gubernacular strands leading the ectopic testis to its deviated position. Others such as Eisendrath,[23] Thompson and Heckel,[50] and Bevan[5] fall in line with this concept.

ANOMALIES OF THE PATHWAY

McGregor[35] was unable to demonstrate such subdivisions of the gubernaculum, stating that nondescent and ectopia can be explained by other anatomic abnormalities. He described an orifice in the inguinal region which he termed the *third inguinal ring*. This ring is distal to the external inguinal ring and serves as the entrance to the scrotal tunnel. If it is absent or underdeveloped, the gubernaculum which guides the testis in its descent fails to make further progress, becomes adherent to the surrounding fascias, and remains only partially descended. On the other hand, the

ninth week of gestation and continues at the high level for the remainder of the pregnancy. Testicular descent fails to occur before the ninth month probably because the testis has not reached a phase of maturation sufficient for response to the gonadotrophin stimulation

Some investigators have concluded that a marked decrease or lack of the hormone—*hypogonadotrophism*—is the causative agent in nondescent, and Dorff[20] tried unsuccessfully to isolate an antihormone to account for cryptorchism. Testicular nondescent does of course occur as part of endocrinopathies such as *hypogonadism*, *hypopituitarism*, *hypothyroidism*, and *hypoadrenalism*

Familial Influences

Nondescent is occasionally familial. Rhodes[42] reported three cases of undescended testes in one family. Brimble-Combe[9] reported bilateral cryptorchism in three brothers. Corbus and O'Connor[18] reported a family of six brothers, four of whom showed unilateral nondescent while the remaining two were bilateral cryptorchids Caucci[14] observed an hereditary influence twice in bilateral cases and six times in unilateral cryptorchism We have observed unilateral cryptorchism in a father and his two sons. In each instance the anomaly was left-sided

Intersexuality

Cryptorchism may actually be a manifestation of a developmental anomaly akin to hermaphroditism During the third month of intrauterine development a mesenchymal bridge, known as the ligamentum latum, is observed connecting the caudal ends of the gonads. In normal development this bridge persists in the female but atrophies completely in the male, thus permitting the testes to descend into the scrotum If the bridge persists, descent is impossible[40,41,42] This type of developmental anomaly is rare Only a few cases have been reported

apparatus which includes, in addition to the testis, the structures of the cord, the inguinal canal, and the scrotum. Lombard[33] concluded that failure of descent is an accentuated manifestation of a neurohormonal disturbance. Robinson and Engle[43] refer to undescended testes with inherent congenital defects and Sohval[48] found dysgenesis in about one-half of the nonscrotal testes. We[15] have described undescended testes with lesions of the seminiferous tubules similar to those observed in pre-adolescent hypogonadism, and have emphasized the fact that such undescended testes can keep pace with the normal only as long as they remain quiescent. As soon as gonadotrophin stimulation (either endogenous or exogenous) is initiated, or as soon as the testis is placed (by orchiopexy) in a position favoring its development, the inherent spermatogenic deficiency manifests itself.

Endocrine Imbalance

The discovery of the close relationship[1] between the anterior lobe of the pituitary gland and the testis focused attention to the pituitary as a cause for nondescent. Soon afterward came the report of Schapiro[45] showing testicular descent in boys following the administration of an anterior pituitary-like hormone derived from the urine of pregnant women, chorionic gonadotrophin This was followed by many clinical papers reporting similar good results Observers such as Winterstein,[56] Lombard,[33] Waugh and Thompson,[54] and Guimarães[26] stated that nondescent is for the most part caused by hormonal imbalance As support for their theory they not only cited the good results that followed hormone administration but pointed to the fact that testicular descent occurs spontaneously during two periods of high gonadotrophin concentration in the circulation—*i.e.*, during the last month of fetal development and at puberty Chorionic gonadotrophin exists in high concentration in the maternal circulation from the seventh or

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SUMMARY

In summary, in the absence of an obvious endocrinopathy, two major causes of testicular retention are listed by most authors. They are either mechanical deterrents to descent or an inherent incapacity of the testis to respond to normal stimuli. Of the mechanical factors, abnormalities of the gubernaculum, which were at one time considered of prime significance, are no longer stressed except to explain the mechanism of ectopic descent. Failure of normal development of the testis, particularly its blood supply, appears to be a more acceptable explanation in view of the fact that a short internal spermatic artery is so frequently the only deterrent to descent discovered at orchiopexy Cremasteric spasticity and actual muscular hypertrophy may be important etiologically, inasmuch as so many cases of pseudocryptorchism result from it. The role of inherent testicular deficiency, vague as this term is, grows in importance with the disclosures of testicular biopsy It is our opinion that a considerable number of instances of cryptorchism are caused by a lack of capacity of the testis to respond to normal gonadotrophic stimulation Some cases of cryptorchism are obviously the result of endocrine dysfunction, but the number of such instances is relatively small (less than 15 per cent in our series).

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SUMMARY

In summary, in the absence of an obvious endocrinopathy, two major causes of testicular retention are listed by most authors. They are either mechanical deterrents to descent or an inherent incapacity of the testis to respond to normal stimuli. Of the mechanical factors, abnormalities of the gubernaculum, which were at one time considered of prime significance, are no longer stressed except to explain the mechanism of ectopic descent. Failure of normal development of the testis, particularly its blood supply, appears to be a more acceptable explanation in view of the fact that a short internal spermatic artery is so frequently the only deterrent to descent discovered at orchiopexy Cremasteric spasticity and actual muscular hypertrophy may be important etiologically, inasmuch as so many cases of pseudocryptorchism result from it. The role of inherent testicular deficiency, vague as this term is, grows in importance with the disclosures of testicular biopsy. It is our opinion that a considerable number of instances of cryptorchism are caused by a lack of capacity of the testis to respond to normal gonadotrophic stimulation Some cases of cryptorchism are obviously the result of endocrine dysfunction, but the number of such instances is relatively small (less than 15 per cent in our series)

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chapter IV

PATHOLOGY

The discussion of the effects of nondescent on the testis may be divided into three sections: (1) histologic appearance, (2) developmental potential, and (3) functional capacity.

HISTOLOGIC APPEARANCE

The literature contains a variety of descriptions of the histologic appearance of the undescended testis, most of them based on a study of testes either removed surgically or obtained at autopsy. The majority of these reports are of adult testes which had been brought into the scrotum at various ages or had been left undisturbed in their undescended position Inasmuch as many of these descriptions reveal a lack of complete familiarity with the prepuberal testis, we concluded early in our study that a reevaluation of the histologic appearance of the normal testis from birth through adolescence was in order Only with the establishment of accurate normal standards could the pathologic aberration be more fully understood

Testicular Biopsy

These studies were carried out through the medium of testicular biopsy Its introduction opened a totally new avenue of approach to the problem of testicular growth and development as well as infertility In the child, observation

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of the histologic changes which occur with increasing age permits establishment of normal standards. Similar studies of the undescended testis affords histologic pictures for comparison with these standards. In the adult, the information gained by the study of the testicular histology yields an accurate picture of the state of spermatogenic

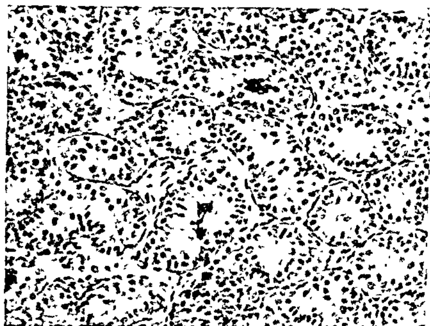


FIG 1 Biopsy of normal testis of boy aged 4 Lumen formation is complete, the cells lining the basement membrane A few of the cells are definitely identifiable as spermatogonia No Leydig cells are observed

preservation In instances of markedly reduced sperm concentration, in the absence of an obstructive lesion, testicular biopsy offers an acceptable method of correlation with semen findings. This is especially true in instances of markedly reduced fertility If the fertility is only very slightly depressed, testicular biopsy may fail to reveal a diagnostic lesion. For instance, men with sperm counts of 20 million or more per cubic centimeter generally yield biopsy specimens which are quite comparable to those with

higher sperm concentrations. In this connection it is interesting to note that, as a result of a large series of semen examinations. MacLeod (37) concluded that the low limit of normal fertility is 20 million per cubic centimeter rather than the previously accepted figure of 60 million per cubic centimeter. The objection that has been offered in regard to the reliability of testicular biopsy—that the small specimen removed at biopsy is not necessarily representative of

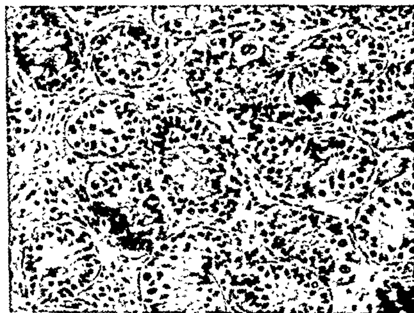


FIG 2 Biopsy of normal testis of boy aged 7 There is slight increase in size of the tubules and a larger proportion of cells have a typical spermatogonial appearance, but in general the picture is quite similar to the 4-year-old testis of Fig 1 No Leydig cells are observed

the entire testis—is not borne out by examination of multiple sections, which generally show remarkable uniformity

Normal Testis

Our study has formulated three phases in the development of the normal child testis

1. Static phase: from birth to age 4 (Fig. 1).

The tubules are small, averaging 66 microns in diameter. They are compactly filled with small, undifferentiated cuboidal cells, a few of which may in the latter part of the phase be identified as spermatogonia. Lumen formation appears. Some of the cells are probably Sertoli cells. Leydig



FIG 3 Biopsy of normal testis of boy aged 10 The tubules are definitely larger Spermatogonia in mitosis as well as primary spermatocytes are observed The intertubular tissue is more abundant with groups of Leydig cells interspersed

cells are present between the tubules in the newborn infant as a result of maternal gonadotrophin, but disappear soon afterward They cannot be identified in a child aged 3½ weeks

2 Growth phase ages 5 to 9 (Fig. 2)

During this period the tubules gradually increase in size, reaching an average diameter of 78 mm Tortuosity appears and lumen formation increases, there is also a more orderly

arrangement of the cells which now line the basement membrane. These cells are now definitely identifiable as spermatogonia and Sertoli cells Leydig cells are not present

3. Developmental or maturation phase: age 10 to puberty. At age 10 a relatively abrupt change occurs, for mitotic figures appear in the spermatogonia and later primary spermatocytes are seen (Fig. 3). At age 11 secondary spermatocytes are observed, and spermatids are numerous

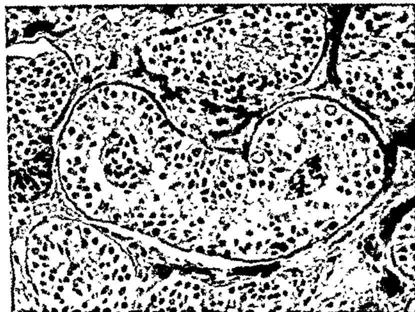


FIG 4 Biopsy of normal testis of boy aged 12 (prepuberal) The tubules are assuming the appearance of the mature adult testis Spermatogonia, primary and secondary spermatocytes, and even spermatids are observed Leydig cells are easily identifiable in the intertubular spaces

at age 12 (Fig 4) Leydig cells first appear in the intertubular spaces at age 10 as a result of endogenous gonadotrophin secretion.

Undescended Testis

REVIEW OF LITERATURE

As stated above, most of the descriptions of the undescended testis are based either on autopsy material or on testes which have been removed surgically. A variety of degenerative changes have been reported, including reduction in quantity or disappearance of all the seminiferous epithelium except the Sertoli cells. When present, the spermatogenic cells are described as showing marked variations from normal, such as irregular shape and poor staining quality. Variable amounts of hyalinization and sclerosis of the membrana propria are reported, occasionally so advanced as to obliterate the lumen completely. The interstitial cells of Leydig are either notably unaffected or are often so hyperplastic that they have been considered by some as the source of malignancy.

The few descriptions of the prepubertal undescended testis are not as uniform. Some investigators[2,5,11] have observed no deviation from the normal testis Others[17,50,65] have described lesions varying from mild increase in the peritubular connective tissue to hyalinization and sclerosis of the membrana propria. Similarly, while some observers have found no impairment of growth of the seminiferous epithelium, others have described developmental and degenerative changes varying from slight reduction of the number of epithelial cells to complete disappearance of all germinal epithelium McGlannan[40] describes three types of undescended testes The first is a small atrophic testis associated with imperfect development of the genital organs, the second presents the picture of a normal infantile testis which fails to develop into the adult type, and the third is one which develops normally at puberty but which undergoes senile changes very early unless it is brought into its normal position in the scrotum

In addition, attempts are made to correlate the degenera-

tive changes with the age of the child and with the degree of nondescent. Cooper,[12] for instance, found a definite correlation with both factors. The younger the child and the further the testis had descended, the more closely did it resemble the normal testis. Along the same line, Pace[51] observed progressive deterioration of the nonscrotal testis with increasing years.

The recent literature based on testicular biopsy has taken advantage of our increased knowledge of the normal testis at a given age so that even minor abberrations from the normal can be readily detected. As a result, our concepts with regard to the age at which degenerative changes begin have changed considerably.

Robinson and Engle[56] found that the undescended testis keeps pace with its normally descended mate only until age 5, thereafter showing retardation of development. They speak of undescended testes as having "inherent congenital defects" but do not elaborate on it. Nelson[48] came to a similar conclusion, setting the age limit at 6 or 7 rather than 5 He stated that after age 6 the seminiferous tubules of the undescended testis show fewer germ cells than are found in the scrotal testis of the same age With increasing age he noted a lag in tubular growth, further reduction in the number of spermatogonia, and thickening of the peritubular connective tissue Leydig- and Sertoli-cell differentiation remains unaffected Finally, Nelson stressed the fact that similar degenerative changes are seen in scrotal testes and that they are then considered to be "testicular defects of a constitutional nature."

Sohval[61] noted dysgenesis in one-half of the cryptorchid testes which he studied, stating that this may be the cause rather than the result of the nondescent He described three types of dysgenesis and laid great stress on the persistence of tubular immaturity as an index of congenital deficiency.

In some instances, however, there is no evidence of testicular dysgenesis In such cases the inimical extrascrotal

environment alone may be responsible for the decrease in number or quality of the spermatogenic elements Sniffen[60] finds "no clearcut morphological difference between the undescended testis and the scrotal gland" before puberty but adds that the structures are smaller, the germ cells less numerous, and that the nuclei show a lag in maturation.

AUTHOR'S OBSERVATIONS

Our own conclusions on the histologic pattern of the undescended testis are based on a study of 45 bilateral biopsies performed on 30 patients. A bilateral biopsy was done on each boy at the time of orchiopexy and was repeated 6 months to 4 years later in 12 instances. Three of the patients each had 3 biopsies In case of unilateral cryptorchism, without evidence of hypogonadism, the normally descended testis was regarded as a control. In bilateral cryptorchism, the standards of the normal testis previously described by us were used as a control.

Age at Which Degenerative Changes Are First Observed. A part of our report[9] describing the normal testis of childhood also included our findings on cryptorchism, in which we stated that there were no recognizable changes in the undescended testis prior to age 10. Nelson's[48] report suggesting age 6 or 7 had already been published and, when Robinson and Engle's[56] data appeared, suggesting age 5 as the upper limit of safety, we paused to re-examine our material By this time, however, additional data on the undescended testis, particularly in the 7-to-9-year-old group, had become available to us Re-examination of our material has not altered our original conclusions

We have observed testicular dysgenesis in about 20 per cent of our cases *(vide infra)*, but have been unable to find any sustained difference between the histologic appearance of the scrotal testis and of the undescended testis up to and including age 9 in the other 80 per cent At this age, the

only intratubular cells present are spermatogonia and Sertoli cells, and these are similar in number and staining quality for both scrotal and undescended testes (Fig. 5). In a few instances, in the 8-to-9-year-old group, we did note a slight thickening of the membrana propria but these changes were not constant.



FIG 5 Undescended testis of boy aged 9, biopsied during orchiopexy The tubules are remarkably well preserved, containing spermatogonia and Sertoli cells Leydig cells are absent There is no discernible histologic distinction between the inguinal testis and its normal scrotal mate

However, at age 10, when the scrotal testis begins to mature, as evidenced by the presence of both spermatogonial nuclei in mitosis and primary spermatocytes, the difference between the scrotal and the undescended testis is unmistakable In the latter, the histologic picture from age 10 onward shows only minimal cellular development or even actual retrogression. Thickening of the membrana propria and peritubular fibrosis become prominent However, the

Sertoli and Leydig cells remain unaltered

At ages 11 and 12, the distinction between the scrotal and the undescended testis is even more marked. An increasing number of the tubules become shrunken and fibrotic while their cellular content appears to diminish (Fig. 6).

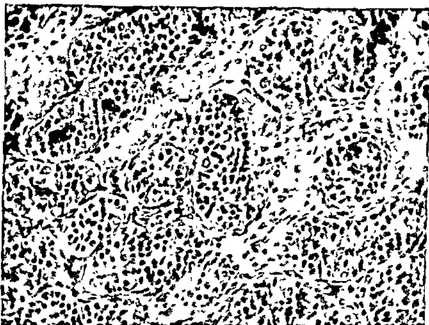


FIG 6 Undescended testis of boy aged 11, biopsied during orchiopexy The tubules are small, slightly fibrotic, and fail to show the maturation usually seen at this age Peritubular fibrosis is evident The Leydig cells appear normal.

At puberty and beyond, the number of spermatogonia in the tubules decreases until, ultimately, only Sertoli cells remain In many instances the size of the tubule, growth of which is most probably dependent on the presence of male sex hormone, continues to increase although the increase does not measure up to that of its scrotal mate As a result there is an apparent rather than an actual reduction in its cellular content (Fig. 7) The appearance of the Leydig cells remains the same for both testes.

The histologic picture presented above refers to those

undescended testes which, we believe, are *inherently normal*, suffering only from their inimical environment. It does not include those testes which have failed to descend because of an endocrinopathy or because of primary hypoplasia. In instances of hypopituitarism the testis lags

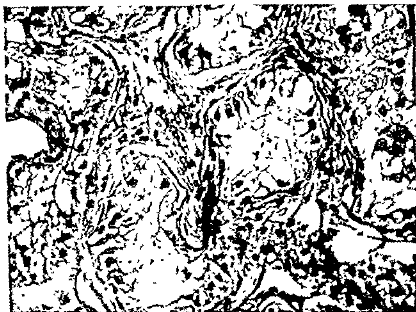


FIG 7 Undescended testis of boy aged 13 (sexually mature), biopsied during orchiopexy The tubules are larger than those of Fig 6, but sclerotic Only Sertoli cells are observed within the lumen Peritubular fibrosis is advanced. There is considerable edema from the recent unproductive administration of 20,000 I U of chorionic gonadotrophin The Leydig cells are normal

in development because of a lack of gonadotrophin stimulation and, in the early stages, presents the appearance of a normal testis of a younger age group (Fig. 8). Such testes may develop normally if they descend spontaneously before age 10, or if they are brought down by gonadotrophin administration, but undergo degenerative changes if they remain undescended

In cases of primary hypoplasia the undescended testis

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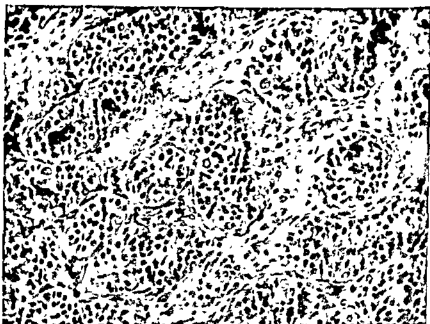


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also explain the discrepancy between the age limit at which degenerative changes of the undescended testis are said to begin: Robinson and Engel, 5 to 6 years, Nelson, 7 years, and our own figures of 9 to 10 years

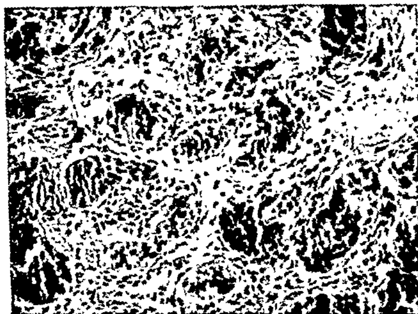


FIG 9 Undescended testis of boy aged 9, biopsied during orchiopexy Grossly it is about half normal size The tubules are small and are compactly filled with *undifferentiated* cells The intertubular space is in part occupied by fibroblasts Leydig cells are not seen Interspersed *among* these tubules are *small islands of relatively* normal (9-year-old) tubules This picture is typical of primary testicular dysplasia

The description of the testis at varying periods following orchiopexy rightly belongs under the heading of results of treatment and will therefore be presented in its proper place.

Position of Undescended Testis with Respect to the Degree of Degeneration In our experience the relative

presents a picture of dysgenesis which is discernible even before age *10*, and which we have previously described as evidence of preadolescent hypogonadism (Fig. 9). Even a small histologic section of such testicular tissue usually presents two distinct pictures: one area shows tubules of

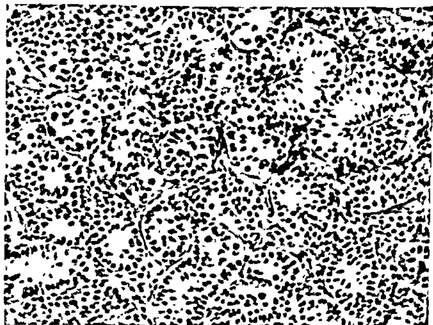


FIG 8 Testis of boy aged 9, biopsied two weeks after the administration of 3,000 I U of chorionic gonadotrophin, which resulted in testicular descent The clinical appearance was that of hypopituitarism The cryptorchism was bilateral The histologic appearance is similar to that of the normal testis of a 2- to 4-year-old boy

normal size but of reduced cellularity, while an adjacent area discloses tubules which are smaller in size, and are compactly filled with small undifferentiated cells In young boys Leydig cells are absent, but in the older age group such testes may contain a full complement of Leydig cells, very often grouped into masses, so as to give an impression of an actual increase in their number About 20 per cent of the undescended testes studied by us present such dysgenesis, which is recognizable as early as age 5 These findings may

CONGENITAL DEFICIENCY

The theory of congenital deficiency, first proposed by Hunter[28] in 1786 and thereafter echoed by many others,[18] was all but forgotten until 1910 when Bland-Sutton[3] called attention to Hunter's work and suggested that failure of descent is the *result* rather than the *cause* of testicular hypoplasia. Other observers[10,14,22,23] subsequently came to the same conclusion, but none of them touched on the nature of the congenital defect. One[65] spoke of nondescent as being a local expression of infantilism, another[26] considered cryptorchism a developmental disturbance, being only the "local expression of a general inferiority"; and yet another[4] attributed the failure of descent to a "faulty developmental tendency of the organism."

A considerable amount of space has been devoted to a description of inadequacy of testicular circulation as a cause of the hypoplasia in cryptorchism.[57] Staemmler[63] described underdevelopment of the testis resulting from hypoplasia and premature sclerosis of the spermatic artery. He demonstrated an endoperiarteritis in small branches of the spermatic artery of undescended testes in young men who had no arteriosclerosis elsewhere. He concluded that although the arterioles of the undescended testis are hypoplastic, they are able to maintain nutrition up to puberty. At this time, the sudden rapid growth of the testis brought on by gonadotrophin secretion overtaxes the hypoplastic arterioles, resulting in sclerosis.

INIMICAL ENVIRONMENT

Those who believe that the undescended testis is normal except for its position follow the line first established by Piana[53] in 1891, who demonstrated degeneration of the testis experimentally transferred from the scrotum into the abdomen. This was later confirmed by many investi-

position—the degree of descent—of the nonscrotal testis has no definite relation to the histologic picture. The lower inguinal testis may and usually does disclose the same degree of degenerative change as the intra-abdominal testis. It is the length of time that the testis remains extrascrotal, i.e. age of patient, that is important. This opinion, as previously emphasized, is in agreement with most authors who have discussed the subject, although others[12,62] conclude that the further the preadolescent testis descends, the more closely does it correspond to the normally located gland at the same age.

DEVELOPMENTAL POTENTIAL

Normal Testis

The designation "normal testis" denotes the existence of a testis containing seminiferous tubules which proceed to complete cellular maturation, with the production of spermatozoa in sufficient numbers to insure adequate fertility. In addition it contains Leydig cells, the maturation of which results in secretion of a sufficient amount of sex hormone to insure the development of normal secondary sex characteristics. These developmental changes occur during puberty which histologically begins as early as age 10, but may not be evident clinically for several years more.

Undescended Testis

A survey of the literature with respect to the developmental potential of the undescended testis again reveals two schools of thought. On the one hand are those who maintain that the retained testis is *congenitally deficient*, lacking the potential for normal development. On the other hand are those who assert that the undescended testis has all the potentiality of a normal one and that it suffers only because of its *inimical environment*.

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INIMICAL ENVIRONMENT

Those who believe that the undescended testis is normal except for its position follow the line first established by Piana[53] in 1891, who demonstrated degeneration of the testis experimentally transferred from the scrotum into the abdomen. This was later confirmed by many investi-

position—the degree of descent—of the nonscrotal testis has no definite relation to the histologic picture. The lower inguinal testis may and usually does disclose the same degree of degenerative change as the intra-abdominal testis. It is the length of time that the testis remains extrascrotal, i e age of patient, that is important This opinion, as previously emphasized, is in agreement with most authors who have discussed the subject, although others[12,62] conclude that the further the preadolescent testis descends, the more closely does it correspond to the normally located gland at the same age.

DEVELOPMENTAL POTENTIAL

Normal Testis

The designation "normal testis" denotes the existence of a testis containing seminiferous tubules which proceed to complete cellular maturation, with the production of spermatozoa in sufficient numbers to insure adequate fertility In addition it contains Leydig cells, the maturation of which results in secretion of a sufficient amount of sex hormone to insure the development of normal secondary sex characteristics. These developmental changes occur during puberty which histologically begins as early as age 10, but may not be evident clinically for several years more

Undescended Testis

A survey of the literature with respect to the developmental potential of the undescended testis again reveals two schools of thought On the one hand are those who maintain that the retained testis is *congenitally deficient*, lacking the potential for normal development. On the other hand are those who assert that the undescended testis has all the potentiality of a normal one and that it suffers only because of its *inimical environment*

testis is aspermatic because the temperature of its abnormal environment is higher than that at which the final stages of spermatogenesis occur.

Rea[55] calls attention to the fact that Moore's experiments were performed on testes that were initially normal, and that regeneration need not necessarily be expected in testes that had *never* been in the scrotum. Jolly and Lieure[29] studied guinea pigs, maintaining the lower half of their body in water baths at various temperatures They found no testicular lesions at temperatures of 40° to 43°C., slight injury to 43° to 46°C., and intense localized lesions at temperatures of 46° to 48°C They confirmed Moore's observations but did not quite accept his conclusions because, as they stated, a temperature of 46° to 48°C is not normally reached within the body of the guinea pig

EFFECT OF HIGH ENVIRONMENTAL TEMPERATURE—
CLINICAL OBSERVATIONS

Clinically, Morgenstern[47] found that acute febrile disturbances cause injury, atrophy, and disappearance of germinal epithelium. Our own observations in humans disclose the fact that the degenerative changes of the undescended testis are not proportional to the height of the temperature in relation to its abnormal position, i.e., an upper scrotal or lower inguinal testis may present the same histologic appearance as an intra-abdominal testis [7]

Applying Moore's methods to humans, MacLeod and Hotchkiss[39] kept their patients' testes warm by insulating the scrotum following which they observed deterioration of the semen They noted also decline of the sperm count to zero approximately three weeks after an illness characterized by a high febrile course Wangensteen[67] examined 35 "testes of men dying of febrile diseases" and observed "a mild degenerative process" in most of them

In summary, it appears that both schools of thought have merit and that a *common meeting ground* might be nearer

gators,[23,31,32,49,58,61] each of whom ascribed a different reason for the deterioration of the seminiferous epithelium. These explanations included injury either to the cremaster muscle or to the testicular nerve supply, obstruction of the excretory ducts of the epididymis, or maintenance of undue pressure on the testis in the inguinal canal.

Effect of High Environmental Temperature—Animal Experimentation. Moore and his associates,[44,45,48] producing experimental cryptorchism by surgically transferring the testis from the scrotum to the abdomen, just as Piana had done, observed intratubular epithelial degeneration identical with that of natural cryptorchism. In order to prove that the epithelial degeneration thus produced was caused by increased environmental temperature of the transplanted testis, they raised the temperature of the scrotal testis either by insulating the scrotum with wool or by applying hot water bottles to it, and were able to reproduce the histologic picture typical of surgically produced cryptorchism. Moreover, they further observed that the altered seminiferous epithelium was restored to normal when the testis was replaced into the scrotum, or when the surrounding scrotal insulation was removed, provided that the deleterious environment had not been maintained too long Finally, they noted that the scrotal temperature was 8°C lower than the intra-abdominal temperature They concluded that the scrotum with its cremaster mechanism is a local thermoregulator for the testis and that tubular degeneration of the undescended testis is the result of its increased environmental temperature

Fukui,[19,20,21] having observed degenerative changes in seminiferous tubules following application of heat rays to scrotal testes, accepted the thermoregulator theory as proposed by Moore *et al.* and emphasized that the bottom of the scrotum, as Moore had stated, is the physiologic place for the testis. Crew[13] added that the imperfectly descended

testis is aspermatic because the temperature of its abnormal environment is higher than that at which the final stages of spermatogenesis occur.

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In summary, it appears that both schools of thought have merit and that a common meeting ground might be nearer

the truth. There is evidence to support the theory of congenital testicular deficiency as well as the theory of unfavorable environment causing the testicular hypoplasia. Complete absence of germinal cells, or their failure to develop beyond a certain stage—dysgenesis—is a not infrequent occurrence in scrotal testes. A large percentage of such congenitally hypoplastic testes may also be involved in the obscure mechanism preventing their normal descent and would therefore not be benefited by the scrotal position, or the hypoplasia may actually be etiologically related to the nondescent. On the other hand, otherwise normally constituted testes may fail to descend at the proper time. The arrest of spermatogenic development in such cases could then be attributed solely to their abnormal position, and proper placement in the scrotum could theoretically be expected to favor normal development.

The large number of orchiopexies being done and the various operative technics that have been devised attest to the popularity of the belief that most undescended testes are abnormal only because of their position.

FUNCTIONAL CAPACITY

Normal Testis

The testis of the newborn contains small seminiferous tubules completely filled with undifferentiated epithelial cells, surrounded by intertubular connective tissue containing distinctly staining Leydig cells. About 5 days after birth, the effect of the withdrawal of the maternal chorionic gonadotrophins becomes evident, resulting in disappearance of the Leydig cells The gland then remains relatively dormant and functionless until it is stimulated by endogenous pituitary gonadotrophins This stimulation begins as early as age 10, as evidenced by the appearance of gonadotrophins in the urine, of mitotic changes in the seminiferous epithelium, and by the reappearance of Leydig cells. It is

minimal and insidious, so that the clinical effect is not demonstrable until approximately age 12. With the onset of puberty the testis assumes the adult role of spermatogenesis and androgen secretion.

Undescended Testis

Inasmuch as the functional capacity of the undescended testis is closely associated with its cellular structure, the foregoing statements relative to the histologic appearance are pertinent to this discussion. The testis has two distinct functions: spermatogenesis and hormone secretion. Because the nonscrotal position affects these two functions differently, a separate discussion of each will lead to greater clarity.

SPERMATOGENESIS

Spermatogenesis is an accurate index of fertility. In the patient with bilateral cryptorchism fertility is directly proportional to the degree of preservation and maturation of the seminiferous epithelium In men with unilateral cryptorchism, however, the normally descended testis may, and generally does, function well enough to insure adequate fertility. For this reason the diagnosis of cryptorchism is much more significant if it is bilateral, and therefore justifies separate discussion

Bilateral Cryptorchism Most authors agree that the adult with bilateral cryptorchism is sterile A few exceptions have, however, been reported Vidal,[66] Burghard,[6] and Marechal[39] found that a large proportion of bilateral cryptorchids are fertile Uffreduzzi[67] observed spermatozoa in 10 per cent of bilateral cryptorchids Monod and Arthaud[42] concluded that nonscrotal testes usually elaborate spermatozoa up to age 20 or 30 Odiorne and Simmons[50] reported fatherhood of a 20-year-old bilateral cryptorchid, in addition to finding normal spermatogenesis in four of nine undescended adult

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of the unilateral cryptorchids He states that unilateral cryptorchids produce an average of one-half as many spermatozoa as normal men. Our own series[7] of over 4,700 infertile men includes only 58 (1.2 per cent) with unilateral cryptorchism. MacLeod[36] found 26 instances of unilateral cryptorchism in an infertile population of 1,425 men (1 9 per cent). Inasmuch as the incidence of nondescent among infertile men is no greater than that of the average fertile male population, it follows that unilateral cryptorchism is not an important etiologic factor in infertility.

In summary, many questions relative to functional capacity remain unanswered, primarily because the paucity of cases precludes statistical analysis Personal communication with other workers, coupled with our own experience, permits the following conclusions which are, however, made with reservations because they are based on an insufficient number of cases·

1. The fertility of otherwise healthy men with unilateral cryptorchism is normal The large sperm population arising from a single testis may be the result of compensatory functional hypertrophy, that is, a larger percentage of seminiferous tubules are taking an active part in spermatogenesis, with fewer tubules remaining in a resting state

2. Unilateral vasectomy results in permanent reduction of the sperm count to one-half of the original level.

3. Unilateral orchiectomy appears to have the same immediate effect but the sperm count ultimately returns to the preoperative level because of compensatory increase of spermatogenic activity, as described above.

HORMONE SECRETION

Here again it is necessary to divide cryptorchism into two distinct categories.

1 Primary cryptorchism includes those patients in whom the failure of descent occurs as an isolated abnormality.

2 Secondary cryptorchism includes those patients who

testes removed at operation. McGlannan[40] found normal spermatogenesis in three of seven undescended testes removed from young adults, and reported fatherhood in a 30-year-old man 18 months after bilateral orchiopexy. Levin[34] reported fatherhood in a bilateral cryptorchid and cited Bergel who saw another such case. Smith[59] described a bilateral cryptorchid who fathered five children.

On the other hand, Hansen[25] reports sterility in nine untreated bilateral cryptorchids, and some improvement of fertility in 11 of 25 bilateral cryptorchids who were subjected to operation. Lanz[33] found spermatozoa in only one of 11 testes that failed to reach the scrotum Griffiths[22] concludes that not only is the bilateral cryptorchid sterile but that the cases reported as fertile had not been sufficiently studied to be accepted as authentic. In any event, the mere fact that fertility in bilateral cryptorchids is so infrequently observed that it merits reporting, is in itself an indication of its exceptional status

Unilateral Cryptorchism Unilateral cryptorchism is encountered four to five times more frequently than bilateral cryptorchism, and here the quality of fertility depends on the state of spermatogenesis in the opposite scrotal testis In those instances in which there is no associated endocrine disturbance and spermatogenesis of the scrotal testis is maintained, fertility is normal On the other hand, if there is an underlying endocrinopathy or some other factor which has prevented normal development of the seminiferous tubules of the scrotal testis, the degree of infertility depends *entirely upon the level of spermatogenesis attained*

There are few reports in the literature on the fertility of unilateral cryptorchids. Hansen[25] reports two series of cases, one of 35 untreated unilateral cryptorchids of whom 11 were infertile, and another of 36 patients with unilateral cryptorchism corrected by orchiopexy, of whom 11 were infertile. Obviously orchiopexy did not improve the fertility

primary bilateral cryptorchids, the androgen excretion was found to be normal although the gonadotrophin excretion was definitely elevated

In summary, the man with primary bilateral cryptorchism has normal secondary sex development including normal libido and potency. His ejaculate is, except on rare occasions, free of spermatozoa. The 17-ketosteroid output usually is normal but may be reduced; the gonadotrophin excretion is uniformly elevated.

Secondary Cryptorchism. Secondary cryptorchism is generally bilateral. It is associated with all the stigmata of the primary endocrinopathy. Sexual maturation is delayed and often incomplete Libido and potency may be reduced. The semen is uniformly azoospermic The 17-ketosteroid and gonadotrophin excretions vary with the type of endocrinopathy.

CONCLUSIONS

The present-day concept of the pathology of cryptorchism is best visualized by dividing cryptorchism into primary and secondary groups Secondary cryptorchism, as the term implies, is a failure of testicular descent resulting from an endocrine disturbance, such as hypopituitarism. The clinical findings of the primary lesion dominate the picture. Histologically, the testis shows a retardation of development commensurate with the degree of endocrine hypofunction. The tubules are smaller and the cellular content is sparser and displays less activity than that of the testis of a normal boy of the same age If the pituitary hypofunction continues beyond puberal age secondary degenerative changes appear, the tubules remain small and hypocellular, and peritubular fibrosis becomes a prominent feature.

Primary cryptorchism may result from inherent testicular deficiency Very often such testes show a characteristic lack of uniformity of the histologic picture. Inter-

are afflicted with an associated endocrine deficiency such as hypopituitarism, hypogonadism, or hypothyroidism. The failure of descent is then merely part of the general endocrine imbalance.

Primary Cryptorchism. Primary cryptorchism is usually unilateral but bilateral idiopathic nondescent is not unusual. In unilateral cryptorchism the contralateral, normal scrotal testis secretes sufficient hormone to maintain an adequate balance. Under such circumstances, all clinical and laboratory tests yield normal values.

In primary bilateral cryptorchism, opinions differ with respect to findings. Experimentally, Ellison and Wolfe[15] noted mild increase in the basophilic elements of the anterior pituitary gland, a reaction similar to though not as severe as that noted following castration. Hanes and Hooker,[24] working on frozen testes, found one-half of the normal quantity of male sex hormone in undescended testes. Perlman[52] observed diminution of testicular cholesterol in the undescended rat testis. Engberg[16] noted reduction of androgen excretion in cryptorchid rabbits similar to but not as marked as that seen in castrated animals.

Clinically, Koch[30] and later Webster[63] noted the presence of androgen in the urine of cryptorchid men Many others[27,41,43,54] reported the presence of normal secondary sex characteristics in cryptorchids From that, they concluded that sufficient hormone was present to insure normal sexual development However, Engberg[16] observed reduction of *androgen excretion in 23 treated and untreated cryptorchid* men (six of these men also had increased gonadotrophin excretion) The fact that only about one-sixteenth of normal testicular tissue is necessary for development of normal secondary sex characteristics makes it clear, as Lipschütz and Ottow[35] have pointed out, why cryptorchid men may have such characteristics even though they have diminished androgen secretion. However, in our own small series of

primary bilateral cryptorchids, the androgen excretion was found to be normal although the gonadotrophin excretion was definitely elevated.

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mingled with the poorly developed tubules described above are islands of even smaller tubules compactly filled with undifferentiated cells. Leydig cells are generally absent but may be observed in the older age groups. This picture is often encountered in scrotal testes of preadolescent hypogonadism[9] and is indicative of reduced developmental potential Our conclusions, based on observation of such boys through puberty and adolescence, are that these testes lack the capacity to develop normally and that they will not produce an adequate number of spermatozoa even if their environment is most favorable.

Primary cryptorchism may, on the other hand, result from a mechanical defect of any of the related structures, the testis per se being basically normal. Under such circumstances, the testicular histology remains relatively normal for at least the first few years. After that, pathologic changes are noticeable

The severity of such a pathologic process varies with the age of the child rather than with the degree of nondescent. We have found that those testes which fail to descend only because of mechanical factors develop normally as long as they remain quiescent, until age 10. At this time, endogenous pituitary gonadotrophin secretion begins and the undescended testis suffers from an incapacity to respond to the stimulation Some observers have described pathologic changes in the testes at an earlier age, 5 or 6, but we have been unable to confirm their findings In any event, if the testis is permitted to remain undescended it suffers irreparable damage because of the increased environmental temperature. The earliest lesion is a lack of cellular differentiation with peritubular fibrosis With increasing age, the failure of tubular maturation becomes more pronounced Tubular growth continues, but at a reduced rate, so that the testis remains small Cellular growth is gradually reduced and ultimately halted, so that the partially enlarged tubule appears relatively empty With further progression

hyalinization and sclerosis become prominent and many tubules become shrunken and fibrosed. During this time Leydig cell development progresses at a normal rate and, because of the reduced tubular size, often appears to be hyperplastic.

The functional capacity of the undescended testis is reflected in the histologic picture. Androgen secretion is maintained at an adequate rate but sperm production is absent. As a result, the adult with primary bilateral cryptorchism yields an azoospermic ejaculate, libido and potentia being normally maintained Adults with primary unilateral cryptorchism generally possess normal fertility.

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chapter V

SYMPTOMS AND COMPLICATIONS OF CRYPTORCHISM

The undescended testis may be and often is involved in pathologic processes similar to those which affect the scrotal testis. Moreover, some of these disorders occur in the undescended testis even more frequently because of the peculiar nature of the anomaly Particularly noteworthy are trauma, torsion, associated hernia, inflammation, and malignant degeneration. In addition, psychic disturbances are said to occur because of a feeling of inferiority resulting from an empty scrotum. Infertility is associated with cryptorchism and is therefore a complication in a true sense However, it has been discussed separately because of its major importance Finally, some anomalies which are part of the clinical picture of infantilism or endocrine dysfunction may be included. Uffreduzzi,[78] whose opinion has been accepted by other observers, stated that retention of the testis is really nothing more than a local expression of infantilism and that it is rarely an isolated feature

SYMPTOMS

Cryptorchism per se is usually asymptomatic However, pain is not an uncommon feature Current literature contains frequent reference to pain associated with cryptorchism, listing a variety of explanations for its occurrence It may result from pressure by structures of the inguinal

canal, from an associated hernia, or from direct trauma to the testis because of its relatively fixed position. Thomson-Walker[50] lists pain as one of the common symptoms, suggesting that it may be an indication for orchiopexy. Ravoth[46] stresses the significance of pain, ascribing it to an associated hernia. However, Schonholzer[51] discounts the relationship between pain and undescended testis, reporting the persistence of pain even after surgical placement of the inguinal testis into the abdomen. Our series includes two patients in each of whom orchiopexy resulted in a small tender testis impinging on the external inguinal ring. Because a normal scrotal testis was present on the opposite side, orchiectomy was done in both instances for the relief of pain.

Torsion of the testis may occur as a complication of cryptorchism. Under such circumstances pain is the most prominent symptom. As a matter of fact, the diagnosis of torsion of the testis should be kept in mind in patients with intra-abdominal testes in whom an acute surgical abdominal emergency develops *(vide infra)*.

COMPLICATIONS

The following are the most commonly encountered complications of cryptorchism: traumatic orchitis, torsion of testis, hernia, inflammation, malignancy, and psychic disturbances.

Traumatic Orchitis

The inguinal testis is more easily traumatized than the scrotal testis because of its relatively fixed position. Lying in intimate contact with the walls of the inguinal canal, it cannot be moved out of danger in the manner in which the scrotal testis is protected by the cremasteric reflex Moreover, contraction of the muscles comprising the inguinal canal subjects the undescended testis to repeated alterations in pressure which, under certain circumstances, may be traumatic and result in pain It may also be one of the

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factors accounting for the greater incidence of malignant degeneration in nonscrotal testes. This is more fully discussed on page 61.

Torsion of Testis

In the scrotal testis, torsion is not an uncommon occurrence. It has a dual pathogenesis, depending on the anatomic anomaly which may be present.

1. *Intravaginal Torsion.* The testis and epididymis are surrounded by visceral tunica vaginalis in such a fashion that the combined organs are loosely connected to the parietal tunica vaginalis by a relatively long mesorchium, thus forming what has been described as a "bell-clapper" deformity.[27] Under such circumstances torsion involves both the testis and the epididymis. Another type of intravaginal torsion may occur if the testis is only loosely attached to the epididymis so that torsion occurs between these two structures.[22]

2. *Extravaginal Torsion.* The testis and epididymis, together with the parietal layer of the tunica vaginalis, take part in the torsion en masse because of mere areolar connections between the parietal tunica vaginalis and the surrounding fascias. In these instances the gubernaculum is either absent or poorly developed.[63] Such torsions generally occur in infants.[17]

In cryptorchism, the anatomic peculiarities described above are the rule rather than the exception so that torsion, both intravaginal and extravaginal, occurs more frequently.

The first description of torsion of the testis by Delasiauve[16] involved an undescended testis. After that many reports of torsion of both descended and undescended testes appeared.[3,5,63] Several excellent resumes have been published, including those of O'Conor,[41] Wallenstein,[60] and

Abeshouse.[1] O'Conor culled from the literature 127 cases of torsion, of which 75 occurred in incompletely descended testes In 150 instances Wallenstein found 90 undescended testes, and Abeshouse collected 153 cases of torsion, 69 of which involved undescended testes. Summarizing all these reports, torsion appears to involve undescended testes almost as frequently as it does scrotal testes. Inasmuch as the incidence of cryptorchism is approximately 0.3 per cent, the frequency of torsion of the undescended testis is rather high. Young[65] states that torsion occurs in one of every 200 (0 5 per cent) nonscrotal testes, but presents no comparable statistics for normally descended testes.

Strangulation of an intra-abdominal testis by a loop of omentum has been reported several times[64] There is also occasional mention of torsion of an undescended testis which had undergone malignant degeneration.[9] In Abeshouse's report, five of 69 testes affected by torsion also had malignant tumors, and Wallenstein's report of 90 cases of torsion of nonscrotal testes included four tumors

Hernia

There is considerable difference of opinion as to the frequency of the coexistence of hernia and undescended testis. Odiorne and Simmons[44] found only 57 per cent of undescended testes associated with hernia, Rawling[47] reported 75 per cent, Uffreduzzi[58] 90 per cent, Schonholzer[51] 93 per cent and Rovsing[49] observed hernias in 100 per cent of his cases of undescended testes This discrepancy probably stems from lack of agreement among the various observers on what constitutes a hernia If the presence of an unobliterated processus vaginalis constitutes a hernia, then hernia is associated with every testis that has not passed beyond the external inguinal ring Such hernias are anatomic rather than clinical For instance, Zuckerkandl[67] found an unobliterated processus vaginalis in 37 of 100 male infants

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Malignancy

The literature on the association of malignancy and cryptorchism is voluminous. For this reason the subject will be discussed separately rather than as another complication of cryptorchism.

INCIDENCE

A few observers[14,38] deny the existence of a direct relationship because they have failed to find frequent linkage of the two pathologic entities. Eccles[19] collected a total of 859 cases of cryptorchism without a single instance of malignancy. Coley[11] had a larger series—1,357 cases with no malignancy.

On the other hand, the Division of Vital Statistics, Washington, D. C., reports malignancy in 3.2 per cent of undescended testes. Hinman and Benteen[29] collected 649 cases of carcinoma of the testes of which 12.2 per cent were undescended. Rubaschow[50] compiled the reports of 21 observers and found 11 per cent of testicular malignancy in undescended testes.[37,40] Many others report statistics varying from 10 to 13.5 per cent of testicular malignancy in cryptorchism. Rea,[48] compiling the reports of six large series, including those of Coley, Cunningham, Odiorne and Simmons, Schischko, Lipschutz, and Dean, found that 136

one to 12 weeks old, but only one of these had a definite hernia.

On the other hand, a hernia may be present even if the testis remains in the abdominal cavity because, as has been stated, the processus vaginalis, preceding the testis in its descent, may reach the scrotum independently and remain unobliterated. A somewhat different concept of the frequent association of cryptorchism and hernia may be obtained from the following statistics: Of a total of 87,000 hernias, 2,262 were associated with undescended testes [11,19,46]

Inflammation of the Undescended Testis and Epididymis

Inflammation of the testis or of the epididymis occurs in the undescended as well as in the scrotal testis

Orchitis is probably not very common because the immature or aspermatogenic testis is *not* subject to inflammation. However, epididymitis and epididymo-orchitis of the undescended testis do occur as complications of prostatitis and may even be accompanied by surrounding cellulitis or abscess. If the intra-abdominal testis is associated with a patent processus vaginalis, epididymo-orchitis may give rise to peritonitis.[63]

Only a few cases of epididymitis have been reported but the complication is probably more common than one would gather from a survey of the literature [2] The reason for this lack of recognition lies in the difficulty of making an accurate diagnosis Canalicular orchitis can usually be easily diagnosed but intra-abdominal orchitis may simulate any acute inflammatory lesion of the abdomen and may evade diagnosis unless the empty scrotum is observed and kept in mind We have seen two instances of epididymitis involving undescended testes. The first was in a young man who developed epididymitis of his single scrotal testis six days after the onset of a gonorrheal prostatitis The next day, with involvement of the undescended testis, he developed contralateral abdominal pain which followed a clinical

course identical with that of the inflammatory scrotal lesion. The second was in a 64-year-old man with benign hyperthrophy of the prostate gland. Preoperative examination revealed an undeveloped, empty left scrotum. The testis was not palpable in the inguinal canal. A suprapubic prostatectomy was done, including section of the accessible vas deferens. His postoperative course was complicated by left-sided lower abdominal pain and elevated temperature, the explanation for which became clear only when he developed stump vasitis on the right side.

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Campbell[6] studied the incidence of association of carcinoma and cryptorchism in 9,741,097 military recruits. His data follow:

0.23 per cent of the recruits developed carcinoma of the testis.

11 per cent of carcinomatous testes were undescended

5 per cent of intra-abdominal testes underwent malignant change.

1.25 per cent of inguinal testes became malignant.

Considering the number of men observed, these figures are quite significant. The ratio of malignancy of the undescended to the scrotal testis is 1:9, while the ratio of undescended to scrotal testes is approximately 1:300, indicating that the undescended testis is about 33 times more likely to become malignant Also, the intra-abdominal testis is at least four times as likely to become malignant as the inguinal one.

DEGREE OF NONDESCENT AND MALIGNANCY

The site of the undescended testis is said to have some relation to the frequency of malignant degeneration Many authors[21,31,51,54,55] are of the opinion that the intra-abdominal testis is less likely to become malignant than the inguinal testis They thus advise placement of the inguinal testis into the abdomen if it cannot be readily brought into the scrotum Lauenstein[36] and Vidal[79] actually taught that transference of the inguinal testis to the abdomen was preferable to its placement in the scrotum because *it functioned well*

in the abdomen, thus simplifying the operation. However, more recently, many instances of malignant degeneration of the abdominal testis have been noted,[5,29,31,59,61,66] all of the essayists concluding, as Campbell did, that the intra-abdominal testis is even more likely to become malignant than the inguinal one. On the other hand, Hofstatter[31] does not believe that there is a higher incidence of malignancy in the intra-abdominal testis than in the inguinal testis. Malignant degeneration of intra-abdominal testes is said to be especially frequent in male hermaphrodites, Zacharias[66] collecting 13 cases and Moehlig[41] adding one more.

Statistics of malignant degeneration of ectopic testes are meager, Klein[35] finding no reference to malignancy of perineal testes.

ORCHIOPEXY AND MALIGNANCY

Orchiopexy has often been advised as a means of preventing malignant degeneration of the undescended testis, but the consensus of most observers is that malignancy occurs just as often in the testis which has been surgically brought into the scrotum as in the untreated, undescended testis Chauvin[10] reports a case of seminoma after orchiopexy but is still of the opinion that the operation lessens the chance of malignant degeneration. DeMoura[15] studied the case histories of young men drafted into the Portuguese army His conclusion, supported by the Portuguese Institute of Pathology, is that orchiopexy does result in a lowered incidence of malignancy, even though it is not a perfectly reliable prophylactic measure

On the other hand, Gordon-Taylor and Till[20] and Warres[62] reported carcinoma many years after orchiopexy Gilbert[24] collected a total of 63 cases of malignancy occurring after orchiopexy and added two of his own Howard[32] reported the case of a man with a scrotal testis which was traumatically dislodged into the inguinal canal and later became malig-

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frequently in the intra-abdominal testis, which is less prone to trauma, than in the inguinal one.

TYPES OF MALIGNANCY IN UNDESCENDED TESTES

The histology of the malignancy is worth noting The most commonly observed lesion is seminoma but other types have been encountered Bramann[4] and Cuneo and Lecene[13] state that malignancy begins in the hypoplastic interstitial cells of the adult undescended testis. Sherwood[73] reported a case of sarcoma of an intra-abdominal testis, but according to Ewing[20] sarcoma of the interstitial cells is rare. Gilbert and Hamilton,[25] dividing the tumors into unicellular and teratoid types, noted that unicellular tumors appeared approximately 12 years after operation while teratoid tumors became recognizable at an average of 5 years after orchiopexy Ontland and Clendening[45] reported a case of an enormous abdominal cyst resulting from a retained testis

The probability is that the type of malignant lesion found in the undescended testis is identical with that occurring in the scrotal testis

Psychic Disturbances

Many clinicians, particularly pediatricians, speak of emotional disturbances encountered even in the sexually immature boy because of the anomalous appearance of the external genitalia caused by an empty scrotum. These disturbances allegedly increase as the boy grows older and come to a climax during puberty and adolescence Cantilo and Speroni[7] report cryptorchism in father and son, pointing out emotional disturbances caused by the implied hereditary factor However, the literature contains very little to substantiate this finding Molitch,[42] analyzing 11 cryptorchid boys who had been institutionalized because of retarded mentality, found no correlation between the cryptorchism and the unstable behavior Davidoff[15] concludes

nant. Carroll[9] analyzed the responses to a questionnaire submitted to 662 urologists It is interesting to note that 77 per cent of them had never seen a case of malignancy in cryptorchism Finding that 270 deaths from carcinoma of the testis occur annually in the United States, of which 9 to 15 per cent arise in nonscrotal testes, Carroll concluded that orchiopexy does not prevent malignancy.

Hinman,[30] noting malignancy after orchiopexy, called attention to the fact that under such circumstances metastasis from the testis extends to the superficial inguinal lymph nodes as well as to the deep ones because the operation has disturbed the normal relationship of lymph channels. We have observed embryonal carcinoma in the testis of a 26-year-old man 13 years after orchiopexy, where the most prominent feature was a superficial inguinal lymph-node enlargement

No reports of malignancy after gonadotrophin administration have appeared, but apparently trauma or other unfavorable environmental factors are not important (*vide infra*) Marlier[39] and Tyrell[57] observed malignancy in testes which had descended spontaneously at ages 16 and 20, respectively Hinman and Benteen[29] state that it is not so much the position of the testis as the biophysical and chemical factors involved in the growth of tissue that are important, and Gerlach[23] concludes that the increased rate of malignancy in the undescended testis is the result of its "basic inferiority."

TRAUMA TO TESTIS AS A CAUSE OF MALIGNANCY

Trauma from muscle contraction is said to be a factor in the frequent relationship of malignancy and cryptorchism. Coley[11] thought that there was a direct relationship in one-third of his cases and Collins[14] found it in two-thirds of the 57 cases which he had observed However, most observers voice the opinion that trauma is grossly overrated as a cause of malignancy, citing the fact that such change occurs more

sents a challenge in diagnosis unless the clinician remains constantly on guard for such an eventuality.

Malignancy occurs about 50 times more frequently in the undescended testis than in the scrotal one, presenting a most serious problem in the management of the anomaly. This is especially pertinent because orchiopexy does not appreciably reduce the incidence of the complication.

Psychic disturbances complicating cryptorchism are considered by some urologists to be serious enough to warrant orchiopexy. It is our opinion that the importance of this factor is overemphasized.

The most important complication of cryptorchism is disturbed spermatogenesis This has already been discussed in Chapter IV, *Pathology*

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that there is no psychic entity associated with cryptorchism.

Our own conclusions are presented with caution because they are based on the observation of a small number of cases and because they are founded on impressions rather than on expert psychiatric technic. We might state, nevertheless, that we have never observed an emotional disturbance in a boy or an adolescent with cryptorchism unless that cryptorchism was part of the symptom-complex of hypogonadism, or unless the patient had been subjected to continuing reminders of the anomaly by repeated visits to physicians. The average adolescent with cryptorchism who experiences normal sexual maturation is either unaware of his defect or is not concerned with it. This reaction is in contrast with that of the boy with normally descended testes who remains sexually immature at a time when his classmates and playmates have developed adult genitalia. Under such circumstances, the feeling of inferiority and the tendency to withdraw from normal activity may be pronounced

SUMMARY

Cryptorchism is generally asymptomatic, being accompanied by pain only in the exceptional case. This pain is usually a signal of the onset of a complication, such as hernia, torsion, or inflammation, but may occur as an unexplained symptom

The undescended testis is subject to complications similar to those encountered in the scrotal testis. These include trauma, torsion, hernia, inflammation, and malignant degeneration In addition, psychic disturbances are said to occur often. Most of the complications are encountered more frequently in cryptorchism because of the nature of the anomaly. The inguinal testis is relatively fixed and is more easily traumatized than the scrotal testis Torsion occurs more readily because the anatomic features favoring it are the rule rather than the exception in cryptorchism Inflammation of the abdominal testis and epididymis pre-

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chapter VI

DIAGNOSIS AND TREATMENT

DIAGNOSIS

Definition

Philologically, the term *cryptorchism* literally connotes the existence of a hidden testicle. Dorland's *The American Illustrated Medical Dictionary* (22nd edition) defines cryptorchism as "A developmental defect in which the testes remain in the abdominal cavity," presumably implying that *those testicles which are halted in their descent in the inguinal canal* technically remain in the abdominal cavity For clinical purposes, the term *cryptorchism* is synonymous with and is embraced by the term *undescended testis,* which in turn denotes that the testis has not come down to its normal position at the bottom of the scrotum

Clinical Diagnosis

The diagnosis of cryptorchism is established whenever physical examination discloses an *empty undeveloped scrotum* The testis may be intra-abdominal in which case it is not palpable, or it may be felt in the inguinal canal It is important that this entity be distinguished from pseudocryptorchism, *ectopic testis, and other associated anomalies*

Differential Diagnosis

PSEUDOCRYPTORCHISM

The diagnosis of cryptorchism would be a very simple matter were it not for the presence of the cremaster muscle

which, when it contracts, may pull a normally descended testis out of the scrotum, thus simulating cryptorchism. In many boys, the cremaster muscle is so hyperactive and the cremasteric reflex so pronounced that testes which are normally situated in the scrotum may be pulled upward during the course of a physical examination. To this deceptive state the term *pseudocryptorchism* has been aptly applied. This entity has long been recognized, and the literature is replete with advice for caution in diagnostic procedures to avoid mistaking it for cryptorchism. The examiner is advised to have warm hands, to make certain that the child is fully relaxed, and to carry out the exmination as gently as possible. If the testis is palpable distal to the external inguinal ring and if it can be pulled into the scrotum, the most likely possibility is a hypertonic cremaster muscle. Testes which appear undescended in a standing position often become scrotally palpable in a relaxed recumbent position. True cryptorchism is associated with an underdeveloped scrotum; the presence of a normal scrotal sac on the affected side should raise the suspicion of pseudocryptorchism.

Many observers, discussing the entity of pseudocryptorchism, have offered the opinion that a large number of the reported successes following gonadotrophin administration resulted from its use in pseudocryptorchids.[62] Bevan[10] found that one-fourth of the patients referred to him because of retained testes did not have cryptorchism because their testes could be manipulated into the scrotum Browne[11] believes that 80 per cent of the nonscrotal testes which he sees are merely retractile. Some clinicians advise the application of heat for its relaxing effect before making a diagnosis of true cryptorchism. Certainly, if there is any doubt, the child should be re-examined when he is less tense and fearful Pseudocryptorchism is not a clinical entity and requires no treatment

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does not agree, concluding that there is no definite evidence to substantiate the gubernacular theory. Some authors[28] believe that ectopia results from an endocrine disturbance and report instances in which the testes became ectopic following prolonged administration of estrogen for carcinoma of the prostate.

Congenital Anomalies Associated with Cryptorchism

If cryptorchism is merely a local expression of infantilism, then its frequent association with other congenital anomalies is to be expected. The literature contains reports of a large variety of such abnormalities. In a series of reports, Rosinsky[60] noted mongolism, cleft palate, hypophyseal growth anomalies, genital hypoplasia, etc. Coley[20] agrees with Uffreduzzi[93] that cryptorchism rarley occurs as an isolated anomaly, and that it is nearly always accompanied by other bodily or mental abnormalities. Hirsch and Jones[41] report a case of pseudohermaphroditism in which the preoperative diagnosis was cryptorchism. Hess[39] collected a series of cases of cryptorchism associated with abnormalities of the central nervous system, including epilepsy, hydrocephalus, and mongolism. Grünfelder and Lasch[32] found a number of associated genital abnormalities, such as hypospadias.

The most commonly found genital anomaly is either separation of the epididymis from the testis by a mesorchium, or the complete separation of the two structures so that the epididymis, lying free, is continuous with the testis only at the hilus.[12] It is this anomaly which predisposes to torsion A few cases have been reported in which the epididymis has preceded the testis in its descent, the former reaching the scrotum, with the latter stopping short in the inguinal canal [92]

Criteria for Treatment

A discussion of the critera for treatment includes the indications, the age at which treatment should be initiated, and the clinical significance of spontaneous descent.

ECTOPIC TESTIS

An ectopic testis is one which becomes aberrant in its descent, ultimately stopping at a point other than the scrotum. Most of such testes take a normal course in their descent through the inguinal canal, deviating from the usual pathway only after they have passed the external inguinal ring.[75] However, instances in which the ectopic testis leaves the abdomen through the obdurator foramen have also been described.

Four types of ectopic testes are said to exist:[44] perineal, superficial inguinal or interstitial, penile, and femoral. A fifth type, not strictly ectopic according to the definition given above, is *ectopia testis transversa* in which both testes are found on the same side of the scrotum. Hertzler[37] has reported 13 such patients, one of whom also had an infantile uterus.

The perineal testicle is the most common variety of ectopia, 105 cases having been collected by 1949.[85] Smook,[74] reporting 12 cases in which the testis lies on the aponeurosis of the external oblique, believes that this type of ectopia is very common. Budinger[12] has also described this anomaly, stating that it is distinguished from the usual form of undescended testis by the fact that the processus vaginalis as well as the testis migrates upward on the aponeurosis of the external oblique Such aberrant migration of both the processus vaginalis and the gubernaculum has also been observed in perineal ectopia [50]

In instances of ectopia as well as in ordinary cryptorchism the epididymis is not in intimate contact with the testis It is abnormally long and thin, being attached to the testis only at its head and merging imperceptibly into the vas deferens.

The cause of ectopia is obscure Most authors believe that the abnormal position results from faulty insertion of the distal end of the gubernaculum. However, Weinberger[88]

does not agree, concluding that there is no definite evidence to substantiate the gubernacular theory. Some authors[25] believe that ectopia results from an endocrine disturbance and report instances in which the testes became ectopic following prolonged administration of estrogen for carcinoma of the prostate.

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INDICATIONS

Consideration of the indications for treatment of cryptorchism must obviously begin with examination of the reasons to correct the anomaly. It is generally agreed that the primary objective is adequate fertility. Additional aims are the prophylactic elimination of a potential focus of malignant degeneration, correction of an associated clinical hernia, and avoidance of psychic disturbances which may arise as a result of the genital anomaly. These items will be fully discussed in Chapter VII. Suffice it to state here that in unilateral cryptorchism which, as already stated, comprises 80 per cent of all cases of cryptorchism, fertility is generally satisfactory. Thus the primary indication for treatment is at once eliminated in this group.

In any event, because results of treatment fall far short of this primary objective and because of the frequency of spontaneous descent, we believe that boys with *uncomplicated, asymptomatic, unilateral cryptorchism should be spared both the hazards and the inconvenience of orchiopexy*. We concede that small doses of gonadotrophin may be administered as a therapeutic test, but warn against the use of large doses, emphasizing the fact that psychic trauma induced during the period of trial therapy may be more harmful than that resulting from the half-empty scrotum. However, many urologists deem it advisable to subject every cryptorchid patient to surgery if other treatment fails

AGE FOR INITIATING TREATMENT

Opinions regarding the most suitable age for initiating treatment to correct cryptorchism have changed considerably in recent years During the early part of the century when little was known of the hormonal factors involved in the mechanism of testicular descent, the sole method of treatment, orchiopexy, was deferred until puberty or thereafter By this age the testes as well as the surrounding tissues were

said to be sufficiently grown to facilitate surgery. Inasmuch as the functional capacity of the testis was judged primarily by its size, consistency, and position, the need for surgical correction at an earlier age was not clearly manifest. These concepts were gradually revised as the surgeon became cognizant of the need for functional as well as cosmetic improvement, and as it became apparent that the nonscrotal testis lost its capacity to develop at least three to four years before the onset of puberty.

During the early part of the century, also, the sole method for appraising the result of orchiopexy was semen examination. However, in unilateral cryptorchism associated with a normally functioning scrotal testis on the opposite side, semen examination is obviously of no value. Even if the undescended testis remains functionless the normally descended one may supply spermatozoa in sufficient numbers to insure adequate fertility. Under such circumstances, semen examination would not disclose the depressed spermatogenesis of the undescended testis either before or after treatment. In bilateral cryptorchism, however, semen examination is applicable. Sterility following bilateral orchiopexy led to a further reappraisal of the methods of treatment, subsequent reports advocating both earlier surgery and improved technics.

Surgery at any age leaves much to be desired, as will be shown in Chapter VII *Results of Treatment.* This accounts for the many modifications of technic, as well as for the several suggested ages for orchiopexy. Winkel-Smith[99] for instance recommends operation before age 2 because the absolute distance from the abnormal testicular position to the scrotum becomes greater with increased growth, and Koop[40] suggests that orchiopexy be done as soon after birth as the diagnosis is established.

With the advent of gonadotrophic hormone treatment, therapeutic concepts were further modified Inasmuch as administration of small doses of the hormone seemed in-

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to puberty and advised postponement of surgery until the sixteenth year. Later analyses were also in general agreement with this concept.[21, 22, 35, 72] In addition, the sobering reports of careful observers who elicited descent in only 20 per cent of treated boys led to further unpopularity of early treatment. Thompson and Heckel[79] came to the conclusion that gonadotrophin administration resulted in descent of only those testes that would ultimately have descended without treatment, and advocated hormone administration merely as a method of distinguishing testes that are destined to descent spontaneously from those that will require orchiopexy. They stated, however, that gonadotrophin administration, even when it fails to effect descent, results in enlargement of the parts involved and thus facilitates subsequent surgery.

TREATMENT OF CRYPTORCHISM

Two methods of effecting descent of the undescended testis have been universally adopted endocrine administration and orchiopexy. Some observers have concluded that neither hormone administration nor orchiopexy accomplishes the aims of treatment. They advocate observation without treatment or, if surgery is indicated for some other reason such as an associated hernia, orchiectomy rather than orchiopexy because removal of the undescended testis eliminates a potential focus of malignant degeneration. Baker[6] goes even further, favoring removal of all high inguinal and abdominal testes for cancer prophylaxis.

Endocrine Administration

EXPERIMENTAL BACKGROUND

The endocrine treatment of cryptorchism had its origin in 1927 with the discovery of a gonad-stimulating principle in the urine of pregnant women.[4, 5, 73] In 1932 Engle[26] injected the immature macacus monkey with extract of human pregnancy urine and noted a marked increase in testicular

nocuous, the tendency to start treatment as soon as the diagnosis was made grew in favor. Moore's experiments,[53, 54] disclosing degeneration of the germinal epithelium of the nonscrotal testis and suggesting that it should be removed from its inimical environment as soon as possible, gave further impetus to the notion of early treatment.

The introduction of testicular biopsy has shed more light on the subject The recognition of physiologic standards disclosed the fact that the normal testis undergoes only slight growth with very little change in its cellular structure up to age 9. At age 10, histologic evidence of maturation first appears. Employing such standards for comparison, Robinson and Engle[63] found degenerative changes in the tubular cells of nonscrotal testes as early as age 5, and advocated initiation of therapy not later than that age. In a similar study, Nelson[55] found degenerative changes in undescended testes in some instances as early as age 6 He was not, however, certain whether the changes were caused by the unfriendly extrascrotal environment or were the result of inherent disease of the germ plasm. In the latter case, degeneration would have taken place even if the testis had been normally situated

Based on our findings, described in Chapter IV, *Pathology*, it is our opinion that, from the age of 10 on, the nonscrotal testis displays a definite lag in development and should no longer be kept in its abnormal position. We believe therefore that treatment should be initiated before age 10 but not necessarily as early as age 5 or 6.

SPONTANEOUS DESCENT

The enthusiasm accompanying the early, favorable results of gonadotrophin administration waned as reports emphasizing the frequency of spontaneous descent were published Johnson[43] reported spontaneous descent in 313 of 541 cryptorchid boys whom he observed over a period of years He suggested the use of endocrine therapy only as an adjunct

hormone-treated cases, concluded that a larger percentage of good results was obtained only by physicians who included pseudocryptorchism in their series. He stated that spontaneous descent, or descent following the use of gonadotrophins, is a rare occurrence in true cryptorchism

The dosage as reported by the various clinicians has also varied considerably Initially, the quantity of gonadotrophin administered was small, doses as small as 100 I.U. twice weekly being reported effective Later, larger doses, averaging 500 I.U. three times weekly were most commonly employed, and a few clinicians administered 500 or 1,000 I.U. daily.

The duration of treatment has also varied considerably. Some observers advise discontinuing gonadotrophin administration if testicular descent fails to occur after 6,000 I.U. have been given, while others advocate the use of as much as 60,000 I.U Perloff[38] reports success with a dosage of 500 I.U. daily for 40 days in boys who had previously been treated unsuccessfully with smaller doses

Anterior-pituitary Extract On the supposition that anterior-pituitary extract would be more effective in inducing descent than pregnancy-urine extract, Hardy, Bigler, and Scott[36] treated 71 cryptorchids with either anterior-pituitary extract or pregnancy-urine extract, or both. Thirty-two boys with 40 undescended testes were given anterior-pituitary extract; 23 boys with 31 undescended testes received pregnancy-urine extract, and 16 boys with 20 undescended testes received both extracts The results were such that they concluded that pregnancy-urine extract administered alone was most effective

Androgen The mode of action of gonadotrophin was presumed to be stimulation of the interstitial cells of Leydig, resulting in production of male sex hormone It was to be expected, therefore, that the administration of testosterone

size as well as descent of the gland from the head of the inguinal canal to the scrotum. He concluded that stimulation by gonadotrophic hormone is the inciting factor in descent of the testis.

CLINICAL EXPERIENCE

Gonad-stimulating Hormone. The first clinical report of the use of the gonad-stimulating principle appeared in 1931 when Schapiro[65] issued the first of his many papers disclosing good results in the treatment of human cryptorchism with pregnancy-urine extract. Many enthusiastic clinical reports of the use of anterior pituitary-like substance (pregnancy urine) appeared, claiming descent of 50 to 75 per cent of undescended testes in patients so treated. Within a few years summaries of clinical experiences with the hormone had appeared, reporting considerable success in inducing descent, especially in bilateral cryptorchism [47, 49]

In 1938 Thompson and Heckel[78] collected a series of 579 cases reported by other observers. Of these, 281 patients had bilateral cryptorchism (562 testes) and 298 had unilateral cryptorchism Testicular descent had been effected by gonadotrophin therapy in 65 per cent of the bilateral cases and in 47 per cent of the unilateral ones However, their experience with this method of treatment was not as encouraging, they treated 29 boys, aged 1 to 15, with 35 undescended testes, and obtained descent in only 27 per cent of the testes As time passed, smaller percentages of success were recorded. Mimpriss,[51] obtaining descent in only 30 per cent of his cases, concluded that gonadotrophin should be employed *only in patients with bilateral cryptorchism associated with subnormal genital development.* In 1939 Thompson and Heckel[79] reported another series, revealing descent in only 20 per cent of testes. In 1941[80] they reiterated that "chorionic gonadotrophin causes descent only of those testes which would descend at time of puberty without treatment." Rea,[62] also reporting descent in 20 per cent of the testes of his

hormone-treated cases, concluded that a larger percentage of good results was obtained only by physicians who included pseudocryptorchism in their series. He stated that spontaneous descent, or descent following the use of gonadotrophins, is a rare occurrence in true cryptorchism.

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Androgen The mode of action of gonadotrophin was presumed to be stimulation of the interstitial cells of Leydig, resulting in production of male sex hormone. It was to be expected, therefore, that the administration of testosterone

would have a similar effect in cryptorchism. Hamilton[32] produced descent in the immature macaque by employing testosterone propionate. In the human, Hamilton and Hubert[34] obtained good results in only three of eight bilateral cryptorchids and in only one of 12 unilateral cryptorchids. *Zelson and Steinitz*.[91] observing complete descent in 23 per cent of bilateral cases and in 15 per cent of unilateral cases following testosterone administration, suggested use of gonadotrophin only in those cases showing partial descent. They credit Denk and Uebelhör[25] with priority in the use of testosterone.

Other Hormones. Thyroid extract has been employed in boys showing evidence of hypothyroidism, as well as in euthyroid obese boys, with only moderate success.

The sex-maturation fraction of the adrenal gland has also been employed in cryptorchism. Pottenger and Simonsen[69] administered the residue of a benzene fraction obtained by the Swingle and Pfiffner method of extracting adrenal glands and obtained descent in eight of nine boys.

Buquet[17] reported favorable results with the use of thymic extracts administered either orally or parenterally.

In conclusion, endocrine treatment of cryptorchism consists of the intramuscular administration of chorionic gonadotrophin in doses averaging 500 I U. three times weekly If descent does not occur after 10,000 I U. have been injected, treatment should be discontinued Small doses of testosterone, from 15 to 30 mg weekly for a total of 300 mg may then be employed, although that is also likely to be ineffective. The use of larger doses of gonadotrophin or androgen leads to premature sexual maturation and should be avoided. The administration of thyroid substance is advisable only in the hypothyroid boy

Orchiopexy

SURGICAL TECHNIC

Surgical placement of the undescended testis into the scrotum was first attempted by Rosenmerkel[67] in 1820. In 1871 Adams[1] attempted orchiopexy on three patients; the first two died and the third underwent unanticipated orchiectomy. Orchiopexy was later performed by Schüller[70] and others, with little success. It thus fell into disrepute until 1899, when Bevan[9] published the results of his improved technic.

Bevan's original description embodies the principle of testicular mobilization which is fundamental to the modern technic of orchiopexy. An abstract of his original report follows:

> An incision 3 inches long is made over the inguinal canal. The external oblique fascia is divided, as are all the coverings of the cord down to the peritoneum The vas deferens and spermatic vessels are isolated and separated from the peritoneum for a distance of 2 to 3 inches within the abdomen. The processus vaginalis is then separated from the cord, ligated at the internal inguinal ring, and divided ½ inch below the ligature. All of the coverings of the cord are removed so that the testicle hangs suspended by the vas and spermatic vessels. A large pocket in the scrotum is made by blunt dissection, care being taken to make the opening in the scrotal neck large enough to admit only the testis which is then placed into the pocket. Closure is carried out according to the Bassini technic for repair of inguinal hernia. In addition, the superficial fascia is sutured to the aponeurosis of the external oblique. This obliterates the areolar space between the superficial and deep fascia in front of the external ring, which is the most likely place for retraction of the testis.

For those cases in which the internal spermatic vessels are too short for scrotal placement, he later[10] recommended bisection of all of the structures of the cord except the vas deferens, deferential artery, and vein

Still later[8] he modified his original technic by placing a

purse-string suture around the neck of the scrotum, superficial to but not surrounding the structures of the cord.

Torek[81,82] added the principle of fixation to Bevan's doctrine of mobilization when he first published his technic of orchiopexy in 1909, crediting Keetley with the prior use of a similar technic. Essentially, the Torek operation consists of "laying bare the testicle, thinning down the cord till it consists of nothing but vas deferens and spermatic vessels, and continuing the dissection of the vessels upward as far as necessary to allow the testicle to come well down without traction." Up to this point the technic is similar to Bevan's. However, Torek now incises the scrotum, brings out the testis, and sutures it to the fascia on the inner surface of the thigh. He then sutures the cut edges of the scrotum to the edges of the thigh incision. This relationship is maintained for from two to three months, after which the testis and scrotum are surgically separated from the thigh

At least fifty modifications of the Bevan and Torek technics have been described All of them are essentially refinements in method to obtain better mobilization or fixation of the testis For obtaining increased testicular mobilization, Bevan's suggestion of cutting the internal spermatic vessels has already been mentioned. La Roque,[48] Yodice,[60] Rosenblatt,[61] and others concentrate on careful dissection of the retroperitoneal space, thus freeing the internal spermatic artery and vein, and permitting the placement of the entire cord in a more direct line to the scrotum With the same purpose in mind, Davison[23] and Gessner[29] suggested transplantation of the cord under the deep epigastric artery and even advised section of the vessels Gross[31] describes a method of extensive retroperitoneal dissection, which permits freeing of the vas deferens down to the base of the bladder and freeing the spermatic vessels well up to the inferior pole of the kidney. By eliminating the inguinal canal he shortens the pathway of the cord considerably He employs rubber-band traction for a few days only to prevent the testis from

slipping back in the early postoperative period (*vide infra*).

Many modifications for fixation of the testis have also been introduced. One advised suture of the gubernaculum, instead of the testis, to the thigh. Wolfson and Turkeltaub[59] detached the gubernaculum after two months, while Ewart[27] insisted on maintaining the attachment for one year. Sargent[67] suggested the use of a single catgut suture between the testis and thigh, thus eliminating the need for the detaching operation. Cotton, linen, silk, and steel wire have been substituted for catgut. Abramson[1,2] suggested attaching the gubernaculum to a fascial flap taken from the thigh. Johner[43] and Chalier[17] advised the attachment of weights to the suture in order to maintain traction Cabot and Nesbit[14] and others modified the traction principle by the use of a rubber band which is attached at one end to the testicular suture, and at the other end, by means of adhesive tape, to the inner surface of the thigh. This allegedly exerts intermittent traction, at the same time permitting more freedom of thigh motion. This method eliminates the disadvantage of direct attachment of the testis to the thigh, either by the Torek technic or any of its modifications, which supposedly induces narrowing of the lumen of the internal spermatic artery as it is stretched This is of course undesirable because it results in a reduction of blood flow through the artery On the other hand, intermittent traction allegedly permits relaxation of the tension and increased blood flow brought about by approximation of the thigh to the scrotum during the shortening phase.

Still other refinements in the technic of fixation have been suggested Petrivalsky[59] and Shoemaker[69] obtain added fixation by placing the testis external to the dartos fascia of the scrotum, that is, between the dartos and the skin. The pocket formed between these two layers is sealed by suturing the opening made in the dartos This can be combined with any of the fixation methods advocated. Ombrédanne[56] described a procedure in which the testis, freed as described above, is

brought through the median raphe of the scrotum and fixed to the opposite thigh. This method of transscrotal fixation has been advocated by many others.[17, 39, 71, 72, 87] Pelle[57] modified the Ombrédanne technic by bringing the testis through the median raphe and then closing the opening in order to prevent return of the testis to the original side of the scrotum. He did not find it necessary to fix the testis to the thigh

The results of orchiopexy will be discussed in Chapter VII, *Results of Treatment*. *Suffice it here to point out that* the many modifications of the surgical technic attest to the dissatisfaction with the end results.

Orchiectomy

Removal of the testis has taken its place as an accepted procedure in cryptorchism. The high incidence of malignancy in cryptorchism has prompted many surgeons to advocate orchiectomy, especially for those patients in whom satisfactory orchiopexy is technically difficult or impossible. A dramatic example of the manner in which a surgeon's opinion may be influenced is found in the report of Szymanowski[76] who in 1868 himself developed carcinoma of an undescended testis and thereafter firmly advocated removal of every nonscrotal testis As early as 1887 Thiriar[77] recognized that the undescended testis is almost always sterile and advised its removal as a prophylactic measure against cancer

In more recent publications Chauvin[19] and de Moura[24] report testicular malignancy after orchiopexy, but they still believe that the operation lowers the incidence of testicular cancer On the other hand, many others[16, 30, 40, 61, 84] conclude that orchiopexy does not reduce the incidence of malignancy in cryptorchism The argument that orchiopexy places the testis in a more accessible position so that malignant degeneration can be detected early appears untenable to us. If the hazard is malignancy, orchiectomy is the only sound procedure Thus, Baker[6] advises removal of the "high

inguinal and abdominal unilateral cryptorchid testis," even if it is found possible to place it in the scrotum.

SUCTION TREATMENT

The application of suction by means of a large syringe in order to "loosen and lengthen" the structures of the cord enjoyed a small measure of popularity in the 1930's. Ballenger *et al.*[7] reported its successful use in 23 patients, in all of whom a testis of normal size was brought into the scrotum. The method never gained popularity, probably because it was realized that only those testes which would eventually have descended spontaneously were brought into the scrotum by suction alone.

OBSERVATION WITHOUT TREATMENT

We are of the opinion that uncomplicated unilateral cryptorchism may be left without further treatment if preliminary doses of gonadotrophin are ineffective. We take this stand for the following reasons:

(a) Men with untreated unilateral cryptorchism are usually fertile. Analysis of our cases of male infertility discloses that the percentage of infertile men with unilateral cryptorchism does not exceed that found in the average population. If the scrotal testis is functioning normally, normal fertility can be assured.

(b) Those observers who have followed by postoperative biopsy patients subjected to orchiopexy agree that a good functional result (normal spermatogenesis) is exceptional. In our series of infertile patients, which is of course not representative of the general population, we were unable to find even moderately satisfactory spermatogenesis in a single adult testis that had been surgically brought into the scrotum before puberty.[18] Moreover, the number of instances in which orchiopexy interfered with the blood supply of the testis, resulting in destruction of the

Leydig cells as well as of the seminiferous tubules, is considerable. Orchiopexy eventuates in testicular atrophy in over 10 per cent of all cases.[31]

(c) Orchiopexy does not reduce the relatively high incidence of malignant degeneration of the undescended testis. Placement of the testis into the scrotum merely because it may be more easily observed is, in our opinion, a poor method of cancer prevention.

(d) Although almost all patients with undescended testes have a patent processus vaginalis, only a small percentage ultimately develop a hernia requiring surgical repair.

(e) We are of the opinion that the importance of the emotional disturbances associated with cryptorchism has been overemphasized. We have observed no such disturbance in our patients and the few reports in the literature find no psychosocial correlation to cryptorchism.

We should like to re-emphasize that the foregoing discussion applies only to instances of unilateral cryptorchism. In bilateral cryptorchism the problem is somewhat different. Although an occasional article reports fatherhood in an untreated bilateral cryptorchid, the number of such instances is so small that it is fair to assume that a bilateral cryptorchid boy will become a sterile adult. Moreover, because bilateral cryptorchism is more likely to result from an endocrine disorder, the indication for intensive hormonal therapy is unmistakable. If the boy appears to be definitely eunuchoid, endocrine treatment should be continued for an indefinite period. On the other hand, if there is no evidence of endocrinopathy the decision with regard to surgical intervention should depend on the size and the position of the testes. If they are intra-abdominal, making a good functional result unlikely, surgery should not be attempted. However, if the testes can be palpated in the inguinal canal orchiopexy should be contemplated. In such instances we are in favor of operating on one side at a time because of the numerous reports of eunuchism following bilateral

orchiopexy. If atrophy occurs after the first operation the advisability of orchiopexy on the other side might well be questioned.

Resume of Treatment

The following is a brief outline of the prevailing, generally accepted methods of treatment.

1. Treatment need not be instituted before age 5 or 6, although we, with many other observers, believe that it may be safely postponed until age 9 From the viewpoint of spermatogenesis, treatment initiated after the onset of puberty is valueless.

2. If there is evidence of endocrine dysfunction, careful and complete study is necessary in order to determine the type and quantity of hormone to be administered.

(a) Chorionic gonadotrophin—This should be administered in relatively large doses (500 to 1,000 I.U.) either daily or three times weekly for a total of 10,000 I U. If signs of sexual maturation, such as growth of pubic hair and enlargement of the penis, appear without progress in the descent of the testis treatment should be discontinued.

(b) Testosterone propionate may be employed, 10 mg. 2 to 3 times weekly, either alone or in combination with the chorionic gonadotrophin. The precautions regarding signs of sexual maturation should be observed even more carefully, inasmuch as the administration of testoserone in excess is known to produce tubular damage

(c) Thyroid extract may be given in doses commensurate with the degree of hypothyroidism Thyroid substance is of no benefit in simple obesity.

3. If there is no evidence of endocrine dysfunction chorionic gonadotrophin may still be used as a therapeutic test in the doses listed above, but overdosage should be avoided

4 If descent does not occur following this regimen the

following alternatives are available: observation without further treatment, orchiopexy, or orchiectomy.

With respect to *orchiectomy,* we are not quite in agreement with Baker who advocates the procedure for all high inguinal and abdominal testes. As stated before, we are more inclined to withhold operation in instances of uncomplicated unilateral cryptorchism. However, if operation is performed because of pain, or because of a symptomatic hernia, orchiectomy is advisable under certain circumstances. For instance, orchiectomy is indicated in a boy with unilateral cryptorchism, if operation discloses an unusually small testis or if satisfactory orchiopexy is technically impossible. Orchiectomy, as a cancer preventative, is the only treatment indicated in the adult with unilateral cryptorchism The alternative is observation without treatment.

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chapter VII

RESULTS OF TREATMENT

Any evaluation of the results of the treatment of cryptorchism is influenced to a large extent by the medical outlook of the physician passing judgment. The pediatrician is interested in eliminating anomalous conditions and in preventing emotional disturbances in his patient, the surgeon wants a good cosmetic result and the repair of a hernia, if present, and many urologists have been overconcerned with the possibility of malignancy in cryptorchids. The promotion of normal spermatogenesis is far from urgent at the time most patients are first seen, and the occasion for follow-up does not generally present itself because of the time-lapse between the treatment and the opportunity for ascertaining the patient's fertility. In consequence, most of the papers reporting good results in the management of cryptorchism make no mention of fertility. Moreover, in instances of unilateral crytorchism, follow-up reports including only semen examination or a history of fatherhood are obviously inconclusive. In cases of bilateral cryptorchism, semen examination is a satisfactory guide in evaluating potential fertility; however, it is necessary to postpone such an evaluation until semen specimens can be obtained On the other hand, testicular biopsy provides an accurate and incontrovertible follow-up method and, to us, is the *sine qua non* in evaluating results of treatment of cryptorchism.

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of spontaneous descent out of a total of 544 cases of cryptorchism, concluding that gonadotrophin should be employed only as an adjunct to oncoming puberty and that orchiopexy should not be done before age 16. Caucci[7] also believed that the administration of chorionic gonadotrophin effects descent only of those testes that would ultimately

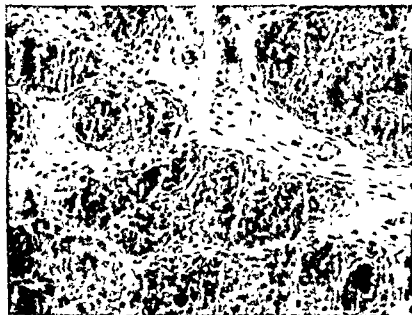


FIG 10. Biopsy of undescended testis which spontaneously descended at age 7. Grossly, it is about one half the size of its normal mate. The tubules are small and are compactly filled with undifferentiated cells. Some areas show a few larger tubules which are normal for age 7 This is a typical picture of dysgenesis (Compare with Fig. 9)

descend without treatment, concluding that hormone therapy actually harms the testis

It is to be noted, however, that even in relatively recent reports, results are judged on descent of the testis rather than on its physiologic function Even semen examination is omitted, and biopsy of such testes has not been reported thus far.

Therapy must be considered under three major headings: spontaneous descent, endocrine treatment, and orchiopexy.

SPONTANEOUS DESCENT

Review of Literature

It is now well recognized that the high incidence of descent reported during the first few years following the introduction of chorionic gonadotrophin resulted from the fact that many of the patients were cryptorchid boys whose testes would ultimately have descended without treatment. In addition, it is likely that many boys with pseudocryptorchism were also subjected to treatment. The recent literature contains numerous examples of such boys who had been rejected for treatment because all that careful physical examination showed was a spastic cremaster muscle which pulled the testis out of the scrotum, especially during examination.[16, 24] Bevan[7] found that 25 per cent of the patients referred to him for operation had testes which could be brought into the scrotum merely by manipulation. Such testes, ultimately assuming a permanent scrotal position, are said to have undergone "spontaneous descent."

The high incidence of cryptorchism at birth (10 to 15 per cent), compared with the relatively low incidence in the adult (0.2 to 0.3 per cent), attests to the great frequency of spontaneous descent. Mimpriss[25] observed it in 25 of 50 cases and concluded that treatment should be withheld from all cryptorchid boys until puberty. Harrenstein[18] studied parallel series, in one the patients received gonadotrophin, while the others were observed without treatment. He observed descent in 50 per cent of each group. Smith[34] observed spontaneous descent in seven of 11 cryptorchid boys whom he followed beyond age 14. He also found an incidence of 3.3 per cent of undescended testes in 511 school boys under 13 years of age and 0.6 per cent in the same group of boys after age 14. Johnson[20] reported 313 instances

its normally descended mate and showed marked degenerative change and peritubular fibrosis (Fig. 12).

Conclusions

Many testes undescended at birth, descend within the first few months of life. As a result, the number of undescended testes falls from 10 per cent at birth to about 1 per cent at age 1. Such testes thus far have not been studied histologically but it may be assumed that most of them are normal because two testes which descended spontaneously



FIG 12. Biopsy of undescended testis which spontaneously descended at age 14 The tubules are smaller than normal, containing only Sertoli cells Tubular sclerosis and peritubular fibrosis are observed Leydig cells are normal

at ages 4 and 6 had a normal histologic pattern. On the other hand, testes which descend spontaneously as late as age 12 show definite evidence of retarded development If we assume that the testes of the two boys aged 12 and 14

Authors' Experience

Five testes which descended spontaneously at ages 4, 6, 7, 12, and 14 have been studied by biopsy. The first two, which descended at ages 4 and 6, showed a histologic picture compatible with the normal for that age. The testes of the remaining three disclosed evidence of hypogenesis or dysgenesis. The testis which descended at age 7 was definitely



FIG 11 Biopsy of undescended testis which spontaneously descended at age 12 The tubules are normal in size but even the healthiest ones contain only spermatogonia and spermatocytes, whereas the normal mate has progressed to spermatid and even spermatozoon formation There is slight peritubular thickening Leydig cells are normal

hypoplastic and probably failed to descend earlier for that reason (Fig. 10) The one which descended at age 12 was relatively normal in size but the biopsy disclosed moderate retardation of development (Fig 11) The fifth testis (in a 14-year-old sexually mature boy) was much smaller than

time the authors had treated 21 boys, only 4 (19 per cent) of whom experienced descent.

Still later, many clinical reports appeared disclosing a large percentage of descent. Hess and Kunstadter[19] treated 39 boys between the ages of 8 and 14, approximately two-thirds of whom had evidence of endocrine dysfunction, and they were able to report descent of 28 testes (71.8 per cent). It is significant, however, that of the 28 descended testes, 25 were in bilateral cryptorchids.

The reports of spontaneous descent in large series of boys who were kept under observation for many years had a sobering effect on the initial enthusiasm for the use of gonadotrophin Soon many papers appeared, reporting descent in no more than 20 per cent of treated patients. In a second review, Thompson and Heckel[37] reported success from gonadotrophin administration in an even smaller percentage of patients, finally concluding that descent had occurred only in those testes that would have descended eventually without treatment. More recently, Browne[5] stated that 80 per cent of the patients referred to him because of cryptorchism actually had merely retractile testes requiring no treatment, and that the other 20 per cent had genuinely undescended testes that could be brought into the scrotum only by operation. Deming[10] summarized the reports of 10 observers, including his own cases Noting that descent had occurred in only 10 of 189 patients treated with gonadotrophin, he concluded that the greatest benefit of hormone administration was that it facilitated surgery by stimulating growth of the testis

Some observers have employed extremely large doses of gonadotrophin in those cases in which usual dosage failed to effect descent Perloff[29] analyzed the case histories of 40 cryptorchids aged 2 to 17 years thus treated Of these, 18 had retractile testes and were at once excluded. One was subjected to orchiopexy without preliminary gonadotrophin treatment Of the remaining 21 boys, 11 had previously

would have descended earlier under hormone administration, we arrive at the logical conclusion that hormone administration should be instituted at an earlier age. However, those testes which fail to descend because of congenital hypoplasia will not benefit by a scrotal position even if it is brought about soon after birth.

RESULTS OF ENDOCRINE TREATMENT

Gonadotrophins

Many endocrine products have been employed in the treatment of cryptorchism, but only one has been universally accepted—chorionic gonadotrophin. The discussion which follows refers to the administration of gonadotrophin *only. The effects of the administration of androgens or other endocrine products is discussed separately.*

REVIEW OF LITERATURE

Gonadotrophin hormone therapy for cryptorchism became widespread after Schapiro's monumental reports [32, 33] His original report, as well as his subsequent ones, covered the treatment of cryptorchids most of whom had other constitutional defects such as hypogenitalism, infantilism, and eunuchoidism Of 32 cases which he reported in 1935, only seven had what we have termed primary cryptorchism He observed descent in 26 of the 32 cases, a few of which received gonadotrophin treatment as long as one year Only three eunuchoid boys were unimproved, the other three, he concluded, were failures because of adhesions

Most of the early reports overflowed with enthusiasm, claiming success in 50 to 100 per cent of the patients treated In 1937, Thompson *et al* [35] reviewed the published experiences of 15 observers, reporting that of a total of 148 cases treated with chorionic gonadotrophin, descent occurred in 106 (72 per cent) Only two papers had appeared reporting success in less than 50 per cent of the cases [1, 31] Up to that

described in Chapter IV. This lack of uniformity of the seminiferous tubules, so widespread that it can be observed even in small histologic preparations, is characteristic of hypoplasia. Its presence, therefore, in testes which have only recently descended into the scrotum is an indication that the nondescent may be etiologically related to the hypo-



FIG 13. Biopsy of testis of boy aged 14, which had descended one year earlier after administration of 10,000 I U. chorionic gonadotrophin Grossly it is smaller than its normal mate Tubules are smaller, containing only spermatogonia and spermatocytes, while those of the normal mate are producing spermatozoa There is a moderate amount of peritubular fibrosis Leydig cells normal

plasia, and that the testis will not benefit appreciably from its scrotal position.

Biopsies were done on two boys in whom descent occurred after 40,000 I.U of gonadotrophin had been given These showed retarded tubular development but unusual stimulation of the Leydig cells (Fig 14), demonstrating again both

been treated unsuccessfully with an average of 10,000 I.U. of gonadotrophin. He administered 500 to 1,000 I.U. of chorionic gonadotrophin daily for from 20 to 66 consecutive days. Sixteen testes (of which three were intra-abdominal) descended in 11 of the 21 boys. Ehrich[11] studied the biopsies of a number of these boys, noting an "interstitial edema and vacuolization of the epithelial cells" but no progress in spermatogenesis. These studies of Perloff and Ehrich are significant because they constitute one of the few observations of the histologic appearance of testes therapeutically brought into the scrotum. They are excellent demonstrations of the inadequacy of intensive gonadotrophin therapy, serving also to emphasize the fact that descent of the testis into the scrotum does not, in itself, constitute a good result.

AUTHORS' EXPERIENCE

In general, our clinical experiences with the use of gonadotrophin for correction of cryptorchism coincide pretty well with those of Thompson and Heckel. We have observed testicular descent in some instances following the administration of chorionic gonadotrophin but believe that these testes would ultimately have descended spontaneously We have had little experience with the large doses of gonadotrophic hormone employed by Perloff and Ehrich, believing that in unilateral cryptorchism such doses may have a deleterious effect on the normally descended testis

Biopsies have been performed by us in 14 patients whose testes descended after the administration of approximately 10,000 I U of chorionic gonadotrophin Of these, two testes descended at ages 2 and 7 and presented normal histologic appearance. The testes of the remaining 12 who were not treated until age 10 to 13, descending after gonadotrophin administration, showed either incomplete development with secondary degeneration (Fig 13) or dysgenesis The latter, consisting of lack of uniformity of the histologic picture, previously observed by us in hypoplastic scrotal testes, is

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FIG. 13 Biopsy of testis of boy aged 14, which had descended one year earlier after administration of 10,000 I U chorionic gonadotrophin. Grossly it is smaller than its normal mate Tubules are smaller, containing only spermatogonia and spermatocytes, while those of the normal mate are producing spermatozoa. There is a moderate amount of peritubular fibrosis Leydig cells normal

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Biopsies were done on two boys in whom descent occurred after 40,000 I U of gonadotrophin had been given. These showed retarded tubular development but unusual stimulation of the Leydig cells (Fig 14), demonstrating again both

the futility of intensive hormone therapy and the all-important difference between *anatomic* and *physiologic* improvement in cryptorchism.

In some testes, especially in those biopsied immediately after descent, a considerable amount of edema was noted,

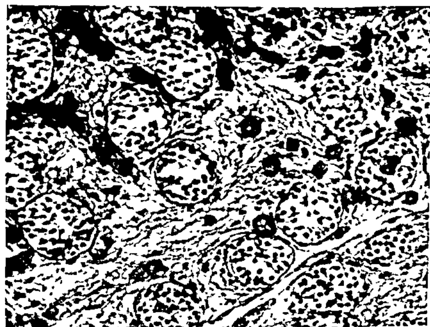


FIG 14 Biopsy of testis of boy aged 11, which descended after administration of 10,000 I U chorionic gonadotrophin Grossly it is much smaller than its normal mate Tubules are very small, containing only undifferentiated cuboidal cells Leydig cells are very prominent and markedly increased in number

probably accounting for the testicular enlargement often seen as a result of gonadotrophin administration (Fig. 15) Such edema was especially prominent in testes which descended after 40,000 I U of gonadotrophin had been given

The Effect of Gonadotrophin Administration on the Scrotal Testis in Unilateral Cryptorchism This depends on the age of the boy, i e, on the capacity of the testis to respond to stimulation, and on the dosage employed In boys

*under age 10 there is apparently no effect on the seminifer-*ous epithelium, then comprising only spermatogonia and Sertoli cells. The enlargement of the testis, often noted as a result of gonadotrophin administration, is caused by edema which subsides soon after the treatment is stopped. After age 10 the seminiferous epithelium responds more

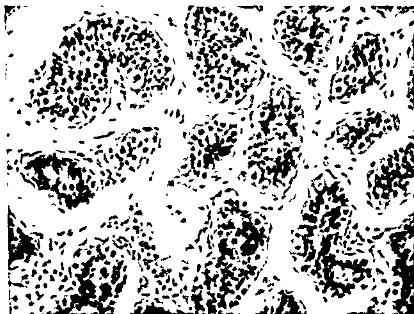


FIG 15 Biopsy of testis of boy aged 19, which descended after administration of 40,000 I U chorionic gonadotrophin Grossly it is very small. Tubules present a picture typical of dysgenesis Spermatogonia are vacuolated, and there is considerable intertubular edema No Leydig cells are present (Courtesy of Dr W E Ehrich)

readily to stimulation, resulting in acceleration of tubular maturation (Figs 16, 17). The premature maturation brought on by exogenous gonadotrophin does not appear to be damaging to seminiferous epithelium, provided that the dosage does not exceed 10,000 I.U

Effect of Gonadotrophins on Testes Previously Brought into the Scrotum by Orchiopexy. Six testes were studied

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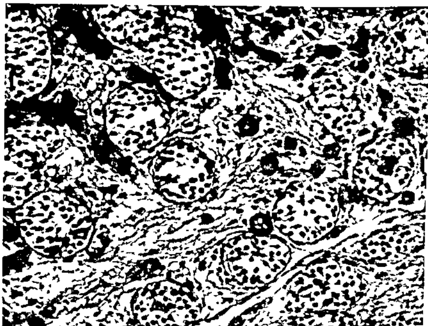


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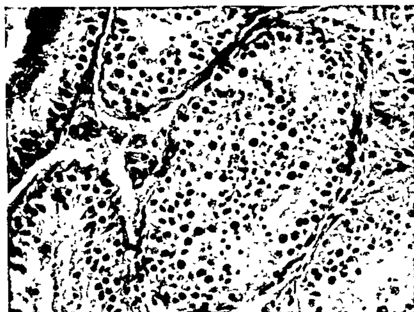


FIG 17. Biopsy of same normally descended testis shown in Fig 16 after administration of 10,000 I U chorionic gonadotrophin Complete maturation is present.

Androgen

Some success has been reported following the administration of androgen[38] and this is particularly significant in that the series contains reports of boys who had been previously treated unsuccessfully with gonadotrophin The administration of androgen to preadolescent cryptorchids is frowned upon by most observers in the belief that androgen is more likely to have a deleterious effect on the seminiferous tubules than gonadotrophin. In actuality, the mode of

after orchiopexy. All were in boys aged 13 to 15 with unilateral cryptorchism who had been subjected to orchiopexy before age 10, after ineffective gonadotrophin therapy. The first biopsy, done several years after operation, disclosed moderately delayed development of the untreated testis and even more retardation of the testis operated upon

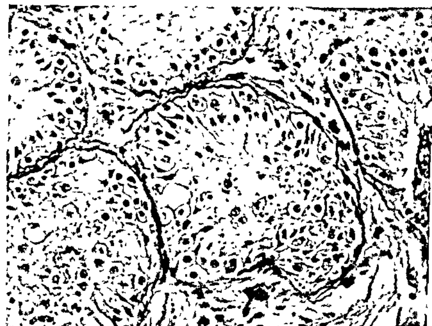


FIG 16 Biopsy of normally descended testis of boy aged 14½ before treatment with chorionic gonadotrophin for contralateral cryptorchism It shows development up to the spermatid stage Leydig cells are normal

(Fig 18) Gonadotrophin administration was then instituted and a second biopsy done after 10,000 I U had been given (Fig 19) In each instance the normally descended testis showed evidence of maturation, whereas the testis subjected to operation disclosed merely an acceleration of the degenerative process similar to that observed in hypoplastic testes at the onset of puberty.[8, 9] This led us to the conclusion that the undescended testis, either *before*

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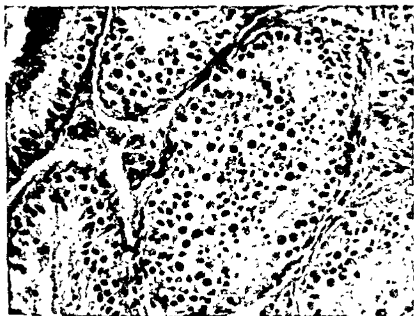


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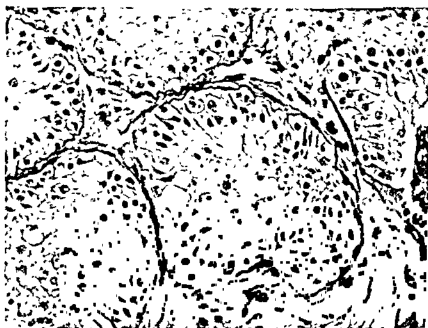


FIG 16 Biopsy of normally descended testis of boy aged 14½ before treatment with chorionic gonadotrophin for contralateral cryptorchism It shows development up to the spermatid stage Leydig cells are normal

(Fig 18). Gonadotrophin administration was then instituted and a second biopsy done after 10,000 I U. had been given (Fig 19). In each instance the normally descended testis showed evidence of maturation, whereas the testis subjected to operation disclosed merely an acceleration of the degenerative process similar to that observed in hypoplastic testes at the onset of puberty[8, 9] This led us to the conclusion that the undescended testis, either before

glycosuria which first appeared during the period of gonadotrophin administration and subsided three weeks after its withdrawal. Thompson and Heckel[36] emphasized the need for avoiding precocious sexual development in youngsters who are psychologically unprepared for it. They advised cessation of hormone therapy before the penis enlarges

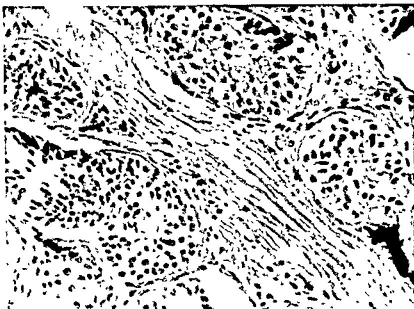


FIG 19 Biopsy of testis shown in Fig 18 after administration of 10,000 I U. chorionic gonadotrophin Compare with Fig 17 Tubules have not increased in size Cellular maturation has actually retrogressed Some peritubular fibrosis is now observed. Leydig cells are normal

Eisenstaedt,[12, 13] finding that hormonal overdosage increases the adhesions around the testis, making surgery more difficult, disagrees with those who believe that hormone administration prior to orchiopexy facilitates the operation. Reporting seven cases of marked testicular degeneration following hormone therapy, he is of the opinion that large doses of gonadotrophin are definitely harmful to the undescended testis. Browne[5], Nelson[28] and many others believe

action of gonadotrophin is probably through stimulation of endogenous androgen secretion, so that the similar effects of exogenous androgen are more direct and therefore more dramatic. We have not employed androgen for the purpose of inducing testicular descent, nor have we had the opportunity to do biopsies on testes so treated.

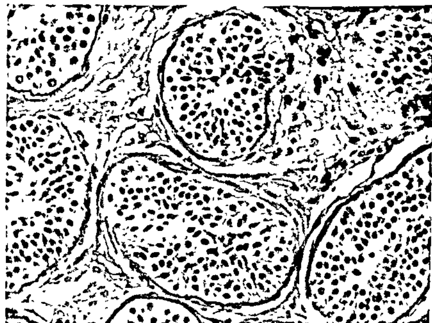


FIG 18 Biopsy of previously undescended testis which had been surgically brought into the scrotum one year earlier (same boy as shown in Figs 16 and 17) It was slightly smaller than its normally descended mate Tubules are slightly smaller but cellular growth and deveopment appear adequate Leydig cells are normal

UNTOWARD EFFECTS OF ENDOCRINE TREATMENT

The complications of hormone therapy that have been reported are numerous but not serious Most of them subside after withdrawal of the hormone Powell[30] reported prostatic hypertrophy during the course of gonadotrophin therapy in a boy of 17, the prostate reverting to normal when treatment was stopped Koplin[22] described a case of

the immature undescended testis that endogenous pituitary gonadotrophin has at the onset of puberty. In unilateral cryptorchism, such premature stimulation probably has a deleterious effect on both testes, but if the administration of gonadotrophin is not prolonged the healthy scrotal testis recovers and does not suffer permanent damage. On the other hand, if the scrotal testis is even mildly hypoplastic

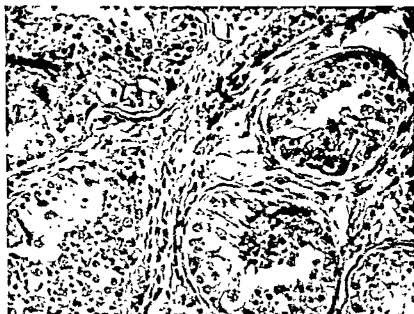


FIG. 21. Biopsy of the same normally descended testis shown in Fig 20 of clinically hypogonad boy aged 13½ after 60,000 I U chorionic gonadotrophin, administered over a period of 16 months. Sexual maturation has occurred but the testis has not developed proportionately. Tubular maturation is retarded and in many places has retrogressed Considerable peritubular fibrosis is present.

the hormone therapy probably hastens the degenerative process in it also (Figs. 20, 21, 22).

Conclusions

It is now generally agreed that gonadotrophin administration promotes descent of only those testes that would ulti-

that the indiscriminate use of the hormone may cause testicular atrophy. There is a possibility, of course, that such testes are initially hypoplastic.

Our own data on this phase are meager and have already been reported partially.[9] If hormone administration is not followed by testicular descent, the testis is inaccessible for

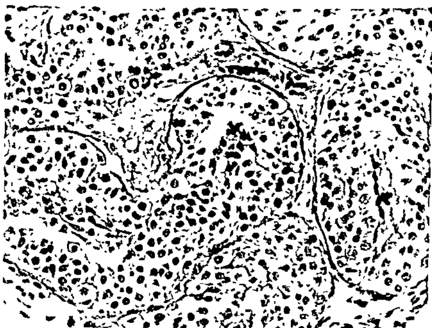


FIG 20 Biopsy of a normally descended testis of a clinically hypogonad boy aged 12½ who had been treated with chorionic gonadotrophin because of contralateral cryptorchism Tubules appear to be normal in size and show undisturbed cellular development, however, other sections of the same tissue show dysgenesis

biopsy Only when operation is performed immediately after hormone withdrawal can the testis be studied histologically, and even then it is difficult to determine the extent of the lesion produced by the nonscrotal environment and the part played by the administered gonadotrophin Based on the few testes studied, our conclusions are that gonadotrophin in large dosage has the same deleterious effect on

surgical problem most often encountered is unduly short spermatic vessels rather than the small size of the testis. Nor can we see any advantage in testosterone administration, which should actually be discouraged because of its acknowledged depressing effect on spermatogenesis.

RESULTS OF ORCHIOPEXY

Review of Literature

The number of modifications in the technic of orchiopexy attests, in itself, to the pervading dissatisfaction with the end results. It is not our intention to discuss the merits of the various technics and modifications thereof which have been suggested. We have culled from the literature the conclusions of many observers with respect to their end results. Moreover, it should be restated that we are interested in functional as well as in cosmetic results, and we consider any report incomplete in which conclusions are drawn only from the postoperative gross appearance, i.e. the size, consistency, and position of the testis. Bevan, for instance, did not hesitate to divide all of the structures of the cord except the vas deferens and its vessels in order to obtain sufficient length for proper placement of the testis into the scrotum. It is now generally agreed that such interference with the blood supply of the testis will not permit the normal development of the seminiferous epithelium. In fact, Cabot[6] states that atrophy of the entire testis results from section of the main vessels. He obtained "good cosmetic results" by resorting to multiple-stage operations whenever it was found difficult to obtain sufficient length in his first attempt at orchiopexy. This was in answer to those surgeons who, despairing of a good cosmetic result from orchiopexy, in difficult cases advised placement of the testis into the abdomen where it would allegedly function at least as well as in the scrotum.[21] Frum[14] reported "good results" of 113 operations performed on army personnel ranging in age

mately have descended spontaneously. As a result, many clinics have discontinued the use of gonadotrophin in the treatment of unilateral cryptorchism. We believe that gonadotrophin administration accelerates the process which eventually results in spontaneous descent, and that it thus serves as both a diagnostic and a therapeutic guide. Doses

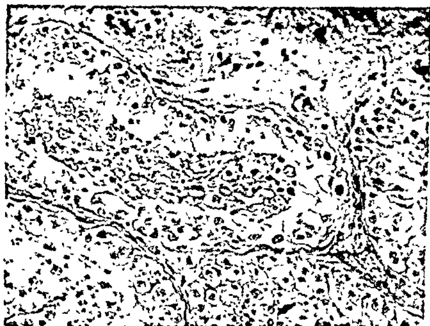


FIG 22 Biopsy of the same normally descended testis shown in Figs. 20 and 21 No treatment has been administered for 5 years Although the testis is grossly normal, tubular deterioration is evident Considerable sloughing of seminiferous epithelium into lumen is seen. There is moderate peritubular fibrosis. The opposite operated testis is small and aspermatogenic The sperm count is 8.4 million per cc

as low as 5,000 I U generally suffice, although as much as 10,000 I U may be safely given. Large doses of gonadotrophin should be avoided because they are injurious to the scrotal testis as well as to the undescended testis. We do not advocate gonadotrophin administration for its stimulative effect on the testis preliminary to orchiopexy because the

He found "definite fertility in 15 and potential fertility in 3 others." In 1956, Gross and Jewett[15] reported a series of 1,222 operations for undescended testes Of these, 38 bilateral cryptorchids were subsequently examined for an evaluation of their fertility and 79 per cent were found to have "acceptable fertility." These are remarkably good results, especially when it is considered that many of the 1,222 orchiopexies were not done until "the prepuberal years" and that all undescended testes, even congenitally hypoplastic ones, are included in their statistical study.

On the other hand, Bishop[4] found few authentic instances of fertility following bilateral orchiopexy. Hansen[17] concluded that testes which had been brought down by orchiopexy almost uniformly lack the capacity to produce spermatozoa Nelson,[27] reporting follow-up testicular biopsies 13 to 22 years after orchiopexy, observed 11 testes in seven patients, four after bilateral and three after unilateral orchiopexy. Of the 11 testes, only two were histologically normal. Of the remaining nine, seven were failures from a spermatogenic viewpoint, two being completely fibrotic. The two satisfactory results were in men who had been subjected to orchiopexy at age 6

Authors' Experience

Our statistics on the end results of orchiopexy are based entirely on histologic study as revealed by testicular biopsy performed many months or years after operation One hundred thirty-two biopsies have been done, of which 73 were on infertile adults who had been subjected to operation before puberty by other surgeons The remaining 59 biopsies were performed by us either at the time of orchiopexy or from four to 24 months after operation

BIOPSY DURING ORCHIOPEXY

These findings have already been reported in Chapter IV. Suffice it to re-emphasize that, in our series, the unde-

from 17 to 30, obviously with no intent to improve fertility, and Keyes and MacKenzie[21] report "excellent results" of 42 orchiopexies in patients whose average age was 19. Needless to state, such surgery may eventuate in a good cosmetic result but it does not promote fertility.

In evaluating functional results of orchiopexy, it is necessary to exclude from consideration operations performed on retractile testes, especially if done in infancy when differential diagnosis is difficult. For instance, Browne[7] found that 80 per cent of the allegedly cryptorchid boys referred to him for treatment had nothing more than retractile testes. He therefore decried the indiscriminate use of hormones and orchiopexy. *We might add that surgery done on retractile testes is not only unnecessary but may be followed by total testicular atrophy.*

Many reports of large series of orchiopexies have been published. Results in these are judged on the size, consistency, position, and mobility of the testis. By some standards, even a testis four-fifths of normal size is considered good. Thus, good or excellent results are claimed for an average of 70 or 80 per cent of all orchiopexies, with an occasional report of 100 per cent success. Semen examination can be employed as an index of success in cases of bilateral cryptorchism only, but even in such cases surprisingly few such reports have appeared. Among those who evaluated the fertility of their patients by semen examination, most admit sterility in all of their cases, although a few make claims of fertility in as many as 50 per cent of their patients.

Two bright exceptions to an otherwise gloomy outlook have appeared, disclosing a high incidence of fertility following bilateral orchiopexy. Both reports, originating in the same clinic and, to some extent, covering the same patients, are therefore logically cited together. In 1935, MacCollum[24] evaluated the fertility of 22 men whom he had subjected to bilateral orchiopexy at least 10 years earlier.

the degree of cell maturation is not as good. Peritubular fibrosis is often widespread and all histologic criteria point to a degenerative process which appears to have been accelerated by the operative procedure. (Figs. 23, 24).

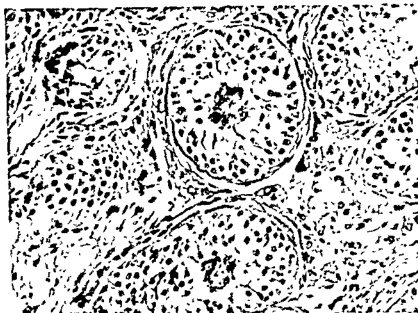


FIG 24 Biopsy of testis shown in Fig 23 4½ months after orchiopexy, when the contralateral scrotal testis had almost fully matured There has been no progress in cellular maturation Some sclerosis and peritubular fibrosis are present Leydig cells are normal

INFERTILITY PATIENTS WITH A HISTORY OF ORCHIOPEXY

In many instances of infertility the exact age when operation was done is not known, except that it was before puberty It matters little in that not a single instance of normal spermatogenesis was observed in the testes operated on Of the 73 biopsies performed in such patients, 16 (8 patients) were in bilateral and 57 in unilateral cryptorchism In the unilateral cases, five had histories and physical findings of epididymitis on the descended side, and the remainder apparently had hypoplasia of even the scrotal testis,

scended testis appears to have suffered little before age 10. However, after that age, definite degenerative changes are observed.

BIOPSY FOLLOWING ORCHIOPEXY

Fourteen testes were subjected to biopsy from four to 24 months after cosmetically satisfactory orchiopexy performed

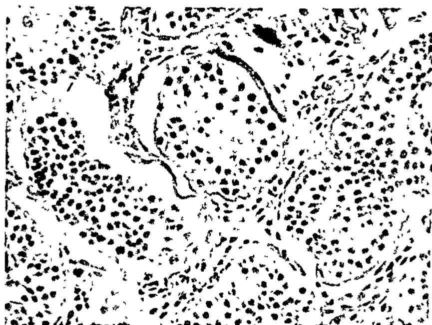


FIG 23 Biopsy of the testis of a boy aged 14 at the time of orchiopexy Grossly, it is somewhat smaller than its normal mate Tubules are smaller and less cellular but cellular maturation appears to have lagged only slightly

by a modified *Bevan* technic. Retroperitoneal rather than cremaster dissection was employed in order to obtain greater length of the spermatic vessels, and attachment to the thigh was employed only to prevent the testis from slipping back during the first week of convalescence Histologically, all appear to have lagged behind in development when compared to the relatively normal scrotal mate The seminiferous tubules are smaller, the cellular content is reduced, and

19 contained tubules with germinal epithelium in various stages of development (Fig. 28). However, in only a few of the tubules of the best-preserved testes did spermatogenesis proceed at a normal rate. Finally, not a single testis could be described as the producer of sufficient spermatozoa to result in fertility.

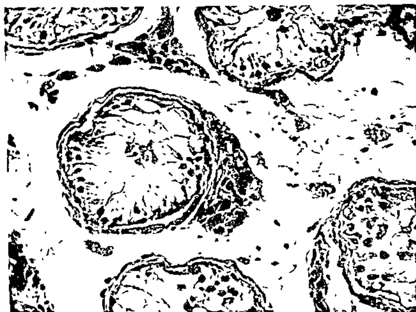


FIG 26 Biopsy of a testis in an infertile adult who had orchiopexy in childhood It is grossly smaller than its hypoplastic scrotal mate. The tubules are small, containing Sertoli cells only Leydig cells are normal

Complications of Orchiopexy

The complications arising from operative intervention for the undescended testis are referable solely to interference with its blood supply. In his early reports, Bevan[2] advocated section of all of the structures of the cord except the vas deferens with its artery and vein in order to permit proper placement of the testis into the scrotum This procedure was found to produce atrophy and it was therefore

accounting for the infertility. Assuming that the undescended testis was also hypoplastic, it can be seen that normal spermatogenesis could not be attained by orchiopexy even if the operative technic were perfect. The histologic picture observed in these patients was uniformly discouraging. Twenty-six of the 73 testes were so small that it was

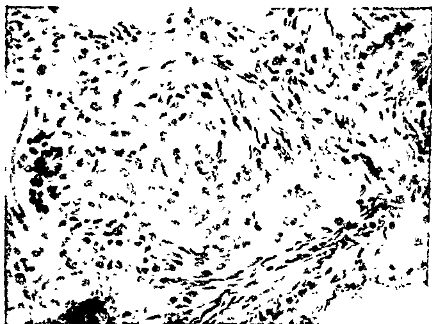


FIG 25 Biopsy of a testis the size of a lima bean in an infertile adult who had an unsuccessful orchiopexy in childhood Fibrosis is present with complete destruction of normal testicular elements, including Leydig cells The patient has bilateral testicular atrophy resulting in eunuchism

obvious from gross examination that spermatogenesis must be absent In each of these, biopsy demonstrated either complete fibrosis with destruction of the Leydig cells, or small, acellular tubules surrounded by normal Leydig cells (Fig 25). Of the remaining 47 testes, 12 disclosed tubules devoid of all cellular elements except Sertoli cells (Fig. 26), 16 showed serious spermatogenic defects consisting of reduction in both tubular size and cellular content (Fig 27), and only

cedures." Correspondence with many surgeons has elicited reports of testicular atrophy following orchiopexy from each one. In our series of 73 testes observed after orchiopexy, 26 were completely atrophied.

In this connection, it is important to emphasize that an undescended testis usually has potentially normal Leydig-

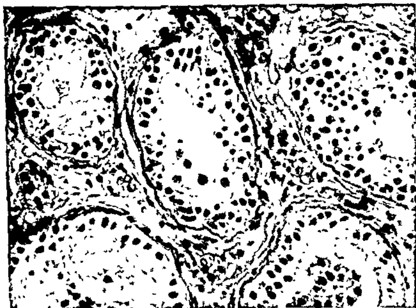


FIG 28 Biopsy of a testis of an infertile adult who had orchiopexy at age 8. Grossly it is slightly smaller than its scrotal mate which has been obstructed by gonorrheal epididymitis An occasional tubule displays normal spermatogenesis but most of them show the spermatogenic arrest illustrated here. There is slight peritubular fibrosis. The sperm count is less than 1 million per cc

cell function, and that atrophy of the entire testis following surgery results in loss of the source of male sex hormone. A child with bilateral cryptorchism is likely to grow up to be a sterile adult, but a child who develops bilateral testicular atrophy following orchiopexy is doomed to eunuchism

Other complications of orchiopexy include (1) pain which occurs if the testis impinges in its new position on the

abandoned. Moreover, even when the cord structures were carefully dissected, instances of testicular atrophy following orchiopexy have been encountered. Only a few surgeons have taken the pains to report such experiences, however. Interference with the blood supply is either intentional, as mentioned above, or accidental. The latter is especially

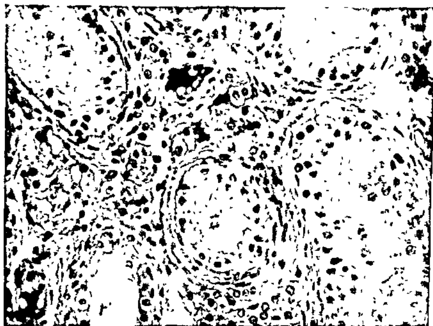


FIG. 27 Biopsy of a testis of an infertile adult who had orchiopexy at age 4 Grossly it is smaller than its moderately hypoplastic scrotal mate Tubules are small and arrested in development at spermatogonium or spermatocyte stage There is moderate proliferation of intertubular tissue with hyperplasia of Leydig cells.

common in the technic which includes complete dissection of all of the cremaster fibers in order to obtain greater cord length.

In his report of biopsy material obtained after orchiopexy, in which he found two of 11 testes completely fibrosed, Nelson[23] opined that it occurred "probably because of interference with the vascular supply during surgical pro-

frequently in the undescended testis, but not often enough to classify the undescended testis as a precancerous lesion. We do not therefore advocate prophylactic orchiectomy, but take issue with those who would place the inguinal testis into the scrotum so that, if malignancy does occur, it will be more accessible for diagnosis. We insist that such a half-hearted procedure is poor prophylaxis and would advise those whose primary aim in the treatment of cryptorchism is avoidance of malignancy to do orchiectomy.

RESUME

1. Many testes which are on cursory examination diagnosed as undescended are in reality pseudocryptorchid, that is, normally descended testes which are pulled up out of the scrotum by undue cremasteric contraction Such boys do not have cryptorchism and require no treatment.

2 Spontaneous testicular descent may occur early in childhood, generally below age 1, but it may occur later. Such instances should be distinguished from true cryptorchism because they need no treatment

3 It is generally accepted that only those testes which would ultimately descend spontaneously, descend after gonadotrophin administration. If this spontaneous descent occurs early, before age 10, or if it is brought about by gonadotrophin administration, the outlook for normal spermatogenesis is good The administration of small doses of gonadotrophin is therefore valuable both as a diagnostic and a therapeutic test

4 The use of large doses of gonadotrophin occasionally results in the descent of a testis which had previously failed to descend However, such testes are uniformly aspermatogenic.

5 Inasmuch as improvement of spermatogenesis is the prime goal of treatment of cryptorchism, orchiopexy is not advised in boys with uncomplicated unilateral cryptochism because such boys usually develop normal fertility even if

newly formed external inguinal ring and (2) recurrent direct hernia.

If malignant degeneration appears after orchiopexy, metastasis usually occurs to the superficial inguinal lymph nodes (which do not normally drain the testis) because the operative procedure has produced an anomalous communication between the superficial and deep lymphatic channels

Conclusions Regarding Orchiopexy

Opinions still differ with respect to the indications for orchiopexy and the age at which it should be done. Influenced by the recent reports of tubular injury after age 6 or 7, many observers advocate surgery at age 6 rather than at the previously preferred age, 10 to 12. We are of the opinion that, if operation is to be done at all, it may safely be postponed until age 9.

On the other hand, we firmly believe that the advisability of performing orchiopexy on boys with *unilateral* cryptorchism is still open to question. Granting that even newer surgical technics will yield a much higher percentage of normal testes, we still question the advisability of performing a "fertility-improving operation" on a boy who will most probably have normal fertility without operation Moreover, up to now, orchiopexy has not only failed to induce satisfactory spermatogenesis but, on the contrary, has resulted in total testicular atrophy in many instances We do not take issue with those who advocate operation in instances of bilateral cryptorchism because, unless so treated, such boys most assuredly become sterile adults Nor do we disagree with those who advocate operation if cryptorchism is associated with symptomatic hernia. We might add, however, that although a patent processus vaginalis is present in almost every instance, very few boys actually develop protrusion of intra-abdominal contents requiring hernial repair

With regard to malignancy, we agree that it occurs more

frequently in the undescended testis, but not often enough to classify the undescended testis as a precancerous lesion. We do not therefore advocate prophylactic orchiectomy, but take issue with those who would place the inguinal testis into the scrotum so that, if malignancy does occur, it will be more accessible for diagnosis We insist that such a half-hearted procedure is poor prophylaxis and would advise those whose primary aim in the treatment of cryptorchism is avoidance of malignancy to do orchiectomy.

RESUME

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3. It is generally accepted that only those testes which would ultimately descend spontaneously, descend after gonadotrophin administration If this spontaneous descent occurs early, before age 10, or if it is brought about by gonadotrophin administration, the outlook for normal spermatogenesis is good The administration of small doses of gonadotrophin is therefore valuable both as a diagnostic and a therapeutic test

4. The use of large doses of gonadotrophin occasionally results in the descent of a testis which had previously failed to descend However, such testes are uniformly aspermatogenic

5 Inasmuch as improvement of spermatogenesis is the prime goal of treatment of cryptorchism, orchiopexy is not advised in boys with uncomplicated unilateral cryptochism because such boys usually develop normal fertility even if

untreated. On the other hand, it is universally agreed that the seminiferous tubules of testes which are retained past puberty suffer irreparable damage. Orchiopexy therefore has no place in treatment of the adult cryptorchid.

6. In the hands of most surgeons, orchiopexy has proved a failure in so far as ultimate spermatogenesis is concerned. However, improved surgical technic is alleged to yield better results. Orchiopexy is thus advised before age 10 in boys with bilateral cryptorchism.

7. Orchiopexy does not reduce the incidence of malignancy of the undescended testis. Although we do not share the view of those who consider cryptorchism a precancerous lesion, we do state with finality that orchiopexy in order to make the testis more accessible for examination is poor cancer prophylaxis.

8. Orchiectomy is not endorsed as a routine treatment for cryptorchism. However, if a small hypoplastic testis is found at operation in a unilateral cryptorchid, removal is more logical than scrotal placement which will not be even cosmetically satisfactory If fear of carcinoma is a major factor, orchiectomy is the only operation indicated. If an adult with unilateral cryptorchism is subjected to operation because of a complication such as hernia, orchiectomy is preferable to orchiopexy

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